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THE RECENT EPIDEMIC OF INFANTILE PARALYSIS.[1]

By Dr. Haven Emerson, New York City.

Since the early summer of 1916 there have been 24,000 cases of infantile paralysis in the United States. Eighteen thousand of these were in New York City and the adjacent territory, in the States of New York, New Jersey, Pennsylvania, Connecticut and Massachusetts, the Borough of Brooklyn being the first to become infected. As an instance of how the infection was spread, I may mention the experiences of three Brooklyn families with 10 children, whose mothers took them each day to Prospect Park to be out of doors. On the 30th of June one child had an acute attack of fever. The family practitioner was called in and prescribed a laxative, light diet and rest in bed for a few days. The child was kept in bed and four days later the mother noticed that he was not able to get up and stand upon his feet. Further rest was prescribed, and at the end of a week the child was able to get up and the case ran on to gradual recovery. Seven days after the onset of the sickness in the first child, one of the other children developed an acute form of fever and weakness of one leg, which was so obvious that the mothers became frightened and took all of the children out of the state into Wayne County, Pennsylvania. Forty-eight hours after arrival the rest of the children came down with the disease and two died. From such examples as this, we should consider that we were dealing with a pretty readily communicable disease, and yet there were many instances in which the disease appeared to be not epidemic in type at all. For instance, in one institution full of children, one case was not followed by any secondary cases.

The distribution was independent of sanitary conditions. There were no cases on Governor's Island, the Federal military station in the harbor of New York. There were 87 children on that island, which was quarantined most effectively at the beginning of the epidemic. Barren Island, situated in Jamaica Bay, is a place to which all the city garbage is brought by boat. All the city's dead animals, often two or three thousand a day, are brought there; it has no public water supply, no sewerage system, the houses have no cellars, no garbage collection, and the people have few garbage cans, the household waste being thrown on the ground about the shanties. There are 1700 people on the island, 350 of them being children, but there was no case of poliomyelitis on that island all summer. Smells, flies and insanitary conditions have prevailed, but because of its geographical position and the social condition of its people, the island is more or less isolated. Where the congestion was least in the city, in the Boroughs of Queens and Richmond, there the cases were most frequent, in proportion to the population.

[1] Read before a meeting of The Johns Hopkins Medical Society, November 6, 1916.

The most constant symptom was found to be the acute onset of fever. The symptom one would think of next in seeing these children would be the change in the character of the child. It becomes more than usually irritable and is unwilling to be fondled and held. If you will analyze that, you will realize that this is the only disease we know of in which the child does not want to be picked up by its mother. In other words, it does not want to be picked up and have its spine flexed anteriorly. It exhibits the so-called spinal sign on flexion.

I feel that we should get along a great deal faster in our general knowledge of this disease if we abandoned the use of the word "abortive." We are dealing with a disease which has paralysis, or which exists without it. It is not uncommon to have a rise of temperature seven days after the onset of the disease, with a sudden development of a paralysis which has not previously existed. These cases were in children admitted to hospitals in the pre-paralytic stage of the disease. We have got the habit of using the terms pre-paralytic, non-paralytic and paralytic. There were many children found with the typical symptoms who never developed a paralysis. I feel that we have no right to consider these as abortive forms of the disease. When those children were examined, they showed all the evidences of a general infection, but it did not go on to a paralysis. To call a case abortive simply because there is no paralysis is apt to cause the physician to feel that he has a patient who is no longer in danger. We must consider that a diagnosis is as important in the absence of paralysis as with paralysis, and the patient an equal, if not a greater danger, as a distributor of the virus.

The experience of our laboratory technicians was that we rarely found a fluid that was not clear, when lumbar puncture was done. If one holds this apparently clear fluid up in the sunlight, the little sparkles that disclose the presence of the cells can be seen, but it looks like clear fluid. In our experience, the fluid was rarely turbid. Under high pressure, with a cell count rising and falling pretty abruptly, one may get the fluid before there is a noticeable increase in the cell count and before the globulin has become noticeable. Again, in a case which has had a doubtful course, one may get the spinal fluid after the time when the cell content has increased, and there may only be the globulin as a guide. The cell count varies considerably, and yet a clear fluid, with an appreciable increase in cell count and globulin has been considered characteristic and diagnostic, when found in a child with the symptoms of an acute febrile infection, even in the absence of any paralysis.

The mortality in this epidemic was much higher than formerly quoted. In the city as a whole the case fatality was 26.96%. In the Borough of Richmond, 19.93%; in the Borough of Queens, 27.99%; in Brooklyn, 21.60%; in the Bronx, 25%; in Manhattan, 28.43%; in Nassau County, L. I., 24%. In the State of New York as a whole, and not including the city, it was 21%, a uniformly higher case fatality than in previous epidemics.

The preventive measures suggested were similar to those given in Osler, the additional advice being given that children should avoid eating uncooked fruit throughout the summer, not because we had any knowledge of danger in uncooked food, but because of the knowledge that most diseases that are carried from person to person may be spread in this way. In order to be quite fair about the milk supply, we took all the cases in Richmond and the Bronx and studied each one as we would have done in the beginning of a typhoid epidemic. No clues indicating that the milk had any influence on the origin or spread of poliomyelitis were found.

There were 4500 cases in the Department hospitals. From the observations which I had a chance to make in the hospitals and from the reports of the physicians in charge, it was evident that no single therapeutic agent proved so useful in giving prompt relief as lumbar puncture. Before there was any general use of adrenalin or the use of normal serum, many cases were treated in our hospitals simply by the withdrawal of spinal fluid, which was often followed by brilliant results. It is only fair to add that there were cases which showed prompt recoveries from severe attacks without any withdrawal of fluid or any other than expectant treatment. Children beginning to develop contractures, and children so uncomfortable they could not sleep, were much helped by warm baths and warm wrappings about their arms and legs. The longer the cases remained in the hospitals and the more the neurologists and orthopedic surgeons studied them, the longer did they postpone any attempt at interference by massage, electricity, or mechanical contrivances on the affected muscles of extremities. The muscles are essentially fatigued and must be rested a long time. It is obvious that many muscles apparently able to take care of themselves are really trying to meet the pull of the strong group on the other side of the lever, which have not been paralyzed.

During the quarantine period, which we have established in New York as eight weeks, the muscles rarely need manipulation of any kind. The opinion has become stronger and stronger throughout the city that premature interference has done more harm than good in the past.

A specific serum has been shown to exist, but that that serum is a curative agent of constant value is quite a different matter. We have had 350 cases treated with the serum of recovered cases, and the results are now being carefully studied.

In the following figures we used the case rate per thousand instead of per hundred for our results:

Borough.	Population.	Poliomyelitis Case Rate Per 1000 Population.
Manhattan	2,634,000	.94
Bronx	575,000	1.16
Brooklyn	1,928,000	2.24
Queens	366,000	3.22
Richmond	97,000	2.92

The most sparsely settled boroughs had rates a little over three times as high as the rate in the Borough of Manhattan and the Borough of Brooklyn, with its tremendous number of cases, had a case rate less than the boroughs of either Richmond or Queens. I have already mentioned the death rate, which shows that the disease took one out of every four patients.

The question comes as to the number of patients we got.

Did we get a complete notification of the disease? This is best answered by a chart prepared by the Department, which shows the number of cases reported and the number we afterwards found to have existed at that time. For instance, on the 8th of June the report came in that a number of babies had been found at the Health Station with paralysis of the arms or legs. These were all in the little district of Brooklyn, the shore front of the Atlantic basin, where the disease started. On the 22d we found three cases reported and later we found there were 26 cases of the disease on that day. That is the margin of error in public health administration. On June 22 we enlisted the help of the lay press and told the people we wanted all the cases of paralysis reported. From that time on there was a general understanding among the public that there was a lot of the disease and people began to do that which is desired by all health officials, *i. e.*, report more cases than there were. When people begin to report cases on suspicion, then you begin to be at the point of controlling the situation. On the 3d of August 239 cases had their onsets, and these cases reached our hospitals 48 hours after the onset of the disease, which is about as close as a department can get to having a case verified and under proper control after onset.

We were of course interested in all sorts of possibilities as to the cause of the epidemic. We thought perhaps the heat might have something to do with the situation, and also the humidity. The only thing we could work out was that the deaths are pretty apt to come coincidently with the height of the humidity, which would be the case with almost any acute infectious disease in little children under five years of age. When one realizes that the deaths are mostly respiratory and that the children are in many instances from poor homes (although the majority did not appear to be in poor condition) the relationship between the humidity and the deaths is pretty obvious. We got little or nothing positive out of these observations on the relation between onset and deaths, and temperature or humidity.

The crude death-rate for the entire city will be only a point or two higher than that of last year. All other infectious diseases have been consistently lower than at any other time in the past five years, for the reason that all parents this summer have taken a great deal more trouble about their children than usual. There have been also a great many things children were spared because the parents were afraid to take any chances this year, in the face of the constant daily advice given by physicians, nurses and others.

Every case of death reported as due to poliomyelitis was followed by a careful investigation, and the descriptions were so simple you could not mistake them. The patients died of failure of respiration in practically all cases (98%). A number died after a prolonged period of unconsciousness and exhaustion, going through what one sees in tuberculous meningitis.

At present, out of every hundred cases reported to us, we are willing to accept as true cases about forty. Out of all the cases we have accepted, 15% showed no paralysis at any time, 18% more showed no paralysis at the end of eight weeks in the hospital, and the rest of them showed paralysis persisting at least until after they had left the hospital. All cases that did not have obvious signs and perfectly clear clinical pictures on admission were kept isolated until the diagnosis was arrived at, and in no instance, in which patients were found on examination to be free from poliomyelitis, did they develop the disease as the result of exposure in the hospital. Further, no doctor and no nurse, either in the field service or in the hospital service, developed this disease during the entire time of the epidemic in New York.

A group that offered an interesting study was that of the children in the institutions in the city. I may say that these institutions in New York City are under the observation of the Department of Health. There are 93 institutions where children are cared for permanently, containing 21,746 inmates; 76 more institutions take children in temporarily, such as day nurseries and summer camps. These take care of 6365 more children, making a total of about 28,000. Among these institutions there were two cases that were properly attributable to conditions in the institutions after quarantine had been established. At the beginning of the epidemic warning had been sent to all these institutions to close their doors against visitors, and that quarantine should be enforced for three weeks for new admissions, before allowing them to mingle with the rest of the children. In St. Joseph's Home, one child developed the disease on the 8th of August simultaneously with the child of the engineer of the institution, who lived outside of the grounds, his house, however, abutting the buildings of the institution, and who had been in the habit of bringing in his child in its carriage each day and keeping it in the garden near the power-house. We had no clue to the person who infected these two children, but as the engineer was a worker in the institution and lived in the house where the other case developed, we suspected he must have played a part. In an institution of 98 children at Huguenot, which was quarantined on July 4, one child developed the disease on August 23. He was unconscious from the time of onset, and remained so for 10 weeks until he died. We did not get an autopsy and the spinal fluid was not characteristic. Nobody could confirm the diagnosis clinically, and yet in the absence of other proof, we must accept this on our list as a case of poliomyelitis. There was a possibility in this case of tuberculous meningitis and also of acute hydrocephalus, but proof was lacking. There are also other clinical possibilities. The unconsciousness with wasting, no sharply localized paralysis and no other confirmatory signs make us suspect that this was not a case of poliomyelitis. We should feel that the isolation of children and the manner of living in the institutions was disadvantageous for the spread of the disease.

The best summary of the whole situation is the report prepared with the approval of the Public Health Association, which met at Cincinnati last week, and which will shortly appear in some of the medical journals. The report is as follows:

The Committee of the American Public Health Association, appointed by the President to report upon the subject of poliomyelitis, begs to submit the following:

The specific cause of poliomyelitis is a microorganism, a so-called *virus*, which may be positively identified at present only by its production of poliomyelitis in monkeys experimentally inoculated. Such experiments have shown this virus to be present not only in the nervous tissues and certain other organs of persons who have died of poliomyelitis, but also in the nose, mouth and bowel discharges of patients suffering from the disease. It has been proved by similar experiments that healthy associates of poliomyelitis cases may harbor the virus in their noses and throats.

These experiments, together with the fact that monkeys have been infected by direct application of the virus to the mucous membrane of the nose and by feeding of the virus, are strong evidence that in nature infection may be directly spread from person to person.

Observations on the occurrence of the disease might seem at first thought to be inconsistent with this conception, since contact between recognized cases can seldom be traced. However, this may be adequately explained by the lack of means for detecting mild non-paralytic cases, and by the belief that healthy carriers of the virus and undetected cases are considerably more numerous than frankly paralyzed cases.

Many facts, such as the seasonal incidence and rural prevalence of the disease, have seemed to indicate that some insect or animal host, as yet unrecognized, may be a necessary factor in the spread of poliomyelitis, but specific evidence to this effect is lacking, and the weight of present opinion inclines to the view that poliomyelitis is exclusively a human disease and is spread by personal contact, whatever other causes may be found to contribute to its spread. In personal contact we mean to include all the usual opportunities, direct or indirect, immediate or intermediate, for the transference of body discharges from person to person, having in mind as a possibility that the infection may occur through contaminated food.

The incubation period has not been definitely established in human beings. The information at hand indicates that it is less than two weeks, and probably in the great majority of cases, between three and eight days.

If the foregoing conception of the disease is correct, it is obvious that effective preventive measures approaching complete control are impracticable, because isolation of recognized cases of the disease and restraint upon their immediate associates must fail to prevent the spread of infection by unrecognized cases of carriers.

These difficulties would appear to be inherent in the nature of the disease. Nevertheless, we may hope for the development of more thorough knowledge which will permit of more effective control of the disease than is now practicable. Of first importance is the more general recognition by practitioners of non-paralytic cases through clinical observation and laboratory procedures.

Lumbar puncture has been shown to offer valuable aid in diagnosis, and a more general use of this test is to be encouraged, since it not only facilitates accurate and early diagnosis, but in many cases affords symptomatic relief as a therapeutic procedure. Without undertaking to predict the future progress of research, we may hope for certain possible developments which may afford far more effective control of the disease, with substantial relief from many inconveniences at present inevitable. Among those possibilities we would include: A practical test for the detection of all clinical types and carriers; a simple and reliable test for distinguishing between susceptible and insusceptible persons; and means of conferring artificial immunity against poliomyelitis.

At present our information demands the employment of the following administrative procedures in attempting to control the disease:

1. The requirement that all recognized and suspected cases be promptly reported.

2. Isolation of patients in screened premises. The duration of infectivity being unknown, the period of isolation must necessarily be arbitrary. Six weeks has been recommended by the Conference of State and Territorial Health Officers with the Surgeon-General of the Public Health Service as sufficient, and this period has been generally accepted throughout the United States.

3. Disinfection of all body discharges.

4. Restriction of the movements of intimate associates of the patient so far as practicable. This should include at least exclusion of the children of the family from schools and other gatherings.

5. Protection of children so far as possible from contact with other children or with the general public during epidemics.

6. Observations of contacts for two weeks after the last exposure.

There is no specific treatment of established value in poliomyelitis. During the persistence of the acute symptoms of the disease, the important principles of treatment are rest in bed, symptomatic relief, and passive support for the prevention of deformities. Active measures during this stage are not only useless but are apt to cause serious and often permanent injury. Hospitalization of patients where possible is to be encouraged. The best chances of recovery from residual paralysis demand skillful after-care, often long continued, and always under the direction of a physician familiar with the neurological and orthopedic principles of treatment. The provision of such after-care often becomes a community problem, demanding the cooperation of all available agencies, social and professional.

DISCUSSION.

Dr. Janeway: After the amount of food for thought that Dr. Emerson has provided us with, it is scarcely fitting for any of us to add our small crumbs to the hearty meal. One thing I would like to add, however, and that is a word of appreciation to Dr. Emerson from an old colleague of his in the Department of Medicine at Columbia for his magnificent work during this past summer. Dr. Emerson started as a physiologist, then came over to us and became a medical man and acquired his interest in public health only somewhat later in his career. Perhaps his medical training has not been without its value to all of us in his recent position in control of this epidemic, because among the things the epidemic will give in the future will be a study of the clinical side

of poliomyelitis on a scale absolutely unparalleled hitherto, largely due to the segregation of such large numbers of cases in the hospitals and to his prompt recognition of the importance of the diagnostic problem in any attempt at control. From the early days of the New York epidemic the diagnosis was in the hands of an extraordinarily competent group of men, all very specially trained in the recognition of the disease. Many facts of clinical importance will unquestionably come out later in their reports.

There are one or two questions I should like Dr. Emerson to answer from his experience if he can. The question of second attacks is one in which I have been much interested. Dr. Holt told me a couple of weeks ago of a fairly conclusive instance of a second attack in a child who had been affected some years previously.

Dr. Emerson did not bring out on the epidemiological side the relation the opening of schools, a point of immediate interest to us in Baltimore, had to the subsidence of the epidemic.

One very striking feature, which anyone who knows New York institutions will recognize, is the extreme difference between this disease and such a one as measles. His report of the existence of only five cases of poliomyelitis in the Foundling Hospital, without the decimation which would always have occurred in an institution of that type if such a disease as measles started. This is one of the problems of the transfer of poliomyelitis by personal contact. That experience seems to me of great importance in determining eventually, as I hope Dr. Emerson will be able to determine, the efficacy of such methods of quarantine as have been adopted in the epidemic during the past summer.

If Dr. Emerson has any time at the end, I should be glad if he could say a little more as to the types of non-paralytic cases, bearing on the question of the possibility of the recognition of these cases. We stand between Scylla and Charybdis. In the presence of an epidemic we are likely to call everything that bears the slightest resemblance to poliomyelitis a proved or almost proved case; and in the absence of an epidemic we are almost certain to fail to recognize cases which are perfectly definite examples of the disease. I am interested especially to know whether definite clinical evidence of meningeal irritation was to be found in almost all of the early cases.

DR. JOHN D. BLAKE, Health Commissioner, Baltimore: The first case of poliomyelitis in Baltimore was reported on July 26. On the 28th of July there was a second case, which came in from Philadelphia. We then went to the mayor for an appropriation for a hospital for these cases, so that there might not be scattered foci throughout the city. As soon as a case was reported it was taken to the hospital. We had but two cases in July, but on the first of August the disease began to increase. We then got in touch with the State Department and insisted on a quarantine. About that time Dr. Ford came back to Baltimore and was of great assistance in establishing the quarantine, which was instituted against New York, Pennsylvania and New Jersey. This was carried out with great difficulty, as people would arrive from outside the state with suspicious cases and the railroads would not take them back, and we had to take care of them until they could be sent home. We also instituted an order that all cases dying should have an autopsy, and no case was decided to be poliomyelitis until it had been so diagnosed by our diagnosticians. There were 186 cases in the city, and there have been 60 deaths to date, a mortality of 34%; 138 of the patients were white and 48 colored. We had 75 white cases before we had one colored, which led us to suspect at first that perhaps the colored race was more or less immune. Six cases were treated at home, where first-class quarantine could be obtained. The results in Baltimore seemed to indicate an infection by contact.

DR. JOHN S. FULTON: The clinical side is so interesting, I hesitate to speak as a public health man. During the second or third weeks in August I imagine the position of Health Commissioner of New York City must have been as unenviable a one as any public health man in this country could have had. A little later there was a public health conference, held in Washington with the Surgeon-General of all the public health authorities in the United States, to which Dr. Emerson was invited. He was good enough to accept the invitation. At that time Dr. Emerson was not personally known to the health officers of all the states of the United States. What he did by appearing at that meeting was to make himself known to these officers and to inspire in them the utmost confidence. That conference was one of the symptoms of the psychosis occurring in consequence of the New York epidemic and Dr. Emerson did very much to settle it and make a beginning of its end.

In Maryland we had had no idea of what it would mean to look after the certification of travel and what the consequences were going to be. We asked the United States Public Health Service to perform this service for us, which they did very gladly and very well, although it was an extremely burdensome thing all round. The certificates were, I think, of some value; at all events the notifications sent out by the U. S. Public Health Service were of use. What the situation in Maryland would have been if we had had an epidemic of poliomyelitis I do not know. Would we have been driven into strict quarantine measures, with border quarantine?

It must be a great satisfaction to Dr. Emerson at this time to think of how many things he has relieved our minds, and what a valuable addition his experiences of the past summer have been to the rest of us, especially his experience with the institutions and on the clinical and hospital management side.

DR. WILLIAM S. BAER: I have been much interested in the epidemic we have had here, particularly as the hospital Dr. Blake took for the treatment of the cases was one with which I was affiliated. We have had an opportunity to study about 104 cases that have come from the city. I was particularly struck with the number of facial cases we had. About 10% of our patients have had simply a facial paralysis. About 10% were cases of paralysis of the respiratory tract.

Turning to the orthopedic side of the question, I will say a few words as to the plan of treatment I think ought to be pursued. The therapeutic side of the treatment still seems to be in doubt as far as the intraspinal injection of fluid is concerned. We have not done any great amount of good in injecting serum either intraspinally or intravenously.

From the orthopedic point of view I have some rather definite ideas. In the first place the treatment would seem to be outlined by the pathological lesions which exist in the spinal cord, so far as the paralytic cases are concerned. In the spinal cord we have the anterior horn cells disabled in three ways—by virus, by effusion, and by hemorrhage. Those cells disabled by effusion are going to recover in a fairly short period of time, say from four to five months. Those cells disabled by hemorrhage will recover more slowly and take anywhere from nine months to a year and a half to recover. The cells poisoned by the virus are not going to recover at all. Consequently the mode of treatment from a surgical point of view is to realize those different stages. In the first stage the case ought to be absolutely at rest for a period of three or four weeks at least. Better, indeed, to put those muscles weakened by disease absolutely at rest, and if necessary to encase not only a limited portion, but sometimes the entire body in some sort of support.

After that period is over, one may begin in those children a mild amount of massage or muscle training. Care should be taken not to overdo the process, as one can do great harm to a weak muscle by trying to make it do too much work. In the second stage of the disease, which lasts anywhere from six months to a year and a half, precautions should be taken against deformities and contractions. During this period electricity and massage are also given, and in addition certain forms of appliances like the

Zander apparatus and Swedish massage should be used. These are much better given in a bath, and particularly given in a warm bath. One can do the work better when one has the buoyancy of the water and the weight is taken off the individual muscles.

The third stage is the operative stage for correction of the deformity. There are two forms of operation, nerve transplantation and muscle transplantation. The first I do not believe offers any hope, as the nerves are probably degenerated. In muscle transplantation in properly selected cases one has a very efficient procedure.

Following this epidemic there will be a great deal of work for the city of Baltimore in assisting in the carrying out of further methods to help these children to help themselves. Two-thirds of them are going to be cripples and a handicap on the city of Baltimore and the state of Maryland. Again, if proper work is to be done for them, proper hospital supervision will have to be provided and the proper amount of money for braces will have to be forthcoming.

Dr. Emerson: There is no one who has been in an official position in this country during the past who will not remember with gratitude the immediate and effective assistance of the officers of the United States Public Health Service. If anything has impressed the public with the necessity of Federal control over many more things than it has now, the experience of last summer should have given the last touch to that impression. There should be a Secretary of Health in the Federal cabinet. There is no question but that the direction of laws and policies should be largely assisted by the kind of service the Federal health officers are giving to localities and communities throughout this country.

I want to pay particular tribute to the physicians in the city of New York who willingly sacrificed their personal health and family practice for the sake of doing what we asked of them in the interests of public health. When you ask physicians in the dull season of the year to notify the Health Department and give over to hospitals their patients, you are asking of them a sacrifice that no other profession is called upon to make.

We could not find any difference in the racial evidences of the disease. It is merely that the colored people are socially isolated from a good many other people in the community. With us the Italians had it first, next the Jews, then the Poles, and the colored people came down last.

In the second week of July we began to have clinics for physicians and we had first-class men coming down to teach them the delicacies and intricacies of the clinical diagnosis of the disease. It was a great clinical opportunity. I believe that up to the present time we have had an instance of paralysis of every one of the cranial nerves.

As to second attacks of the disease, I personally know of none. I have not heard any such cases mentioned.

With regard to the question of opening the schools, I kept a record of poliomyelitis occurring in children between the ages of 6 and 14 during the first few weeks of school. We have a school population of 1,000,000 children. In the two weeks between the 17th of September and the 1st of October we had in the first week 16 children of school age with poliomyelitis, and in the second week, 18 children. The week before school opened we had 16 cases; the week school opened we had 18 cases; the second week, 16 cases; the third week, 5 cases; the fourth week, 5; the fifth, 11; the sixth week, 7; and the seventh week, 6 cases. There is no record that this disease becomes epidemic in schools. It does not pass readily under these conditions. We would have felt justified in opening the schools on time, but we could not influence public opinion to that extent.

It was interesting to see that in the hospitals, possibly owing to the season of the year, there was no epidemic among the 4500 taken from their homes. We had an occasional case of measles and a few of whooping cough, but none of the secondary cases of acute infectious disease such as usually come into hospitals for children under five.

With regard to the recognition of pre-paralytic cases I can add very little. The recognition will, of course, be more likely during an epidemic than at other times, and until we have a specific diagnostic test, we must trust to the clinical acumen and judgment of physicians of large experience. There are many able physicians in New York who feel that the spinal puncture is as nearly a specific test as we want, and that, taken with the clinical picture, it forms a very valuable aid. At present it is quite impossible for anyone to say positively that they have got a true non-paralytic case of the disease. The opinion is strong within the Department of Health that with a paralytic case and other children coming down without paralysis in a family or house you have a right to call such coincident cases "infantile paralysis."

As to meningeal irritation, it is worth while to remember the old English name of the disease "morning paralysis," derived from the fact that patients may go to bed perfectly well and wake up with the disease. I remember perfectly well seeing a boy going to work, who tripped and fell, picked himself up and fell again, and who had to be helped home. He obviously had no meningeal irritation and yet developed a typical and severe paralysis in the midst of apparent perfect health.

We had facial paralysis in about 25% of our patients.

The after-care of these patients has been given a great deal of attention in New York. We have a permanent central committee on after-care, and a so-called fund for braces, which is really used for all kinds of needs of these children. Every case on discharge is visited at once by a nurse, and in the central office of the after-care committee a record is kept of every case, so that some years from now we will know what the particular care of each child has meant. We have in the community now about 5000 children with a persistent paralysis. Six hundred of these will be almost permanently bedridden. Two thousand five hundred of them are unable to walk now and they must be taught, like the cardiac and the handicapped tuberculous patient, to work at a trade which will give them self-support.

The medical relief, the transportation, the hospital and dispensary care, the home visits and the education for self-support are all to be directed by the committee on after-care, which has the support and assistance of all the important medical and social relief agencies in the city.

JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly. Volume XXVIII is now in progress. The subscription price is $2.00 per year. (Foreign postage, 50 cents.) Price of cloth-bound volumes, $2.50 each.

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POLIOMYELITIS CITY OF NEW YORK CASES AND DEATHS REPORTED
JUNE JULY AUGUST SEPTEMBER OCTOBER
CASES BY ONSET
REPORTED CASES
REPORTED DEATHS

FIG. 1.—Cases and deaths reported, July to September, 1916.

FIG. 2.—Distribution of cases in the Borough of Manhattan.

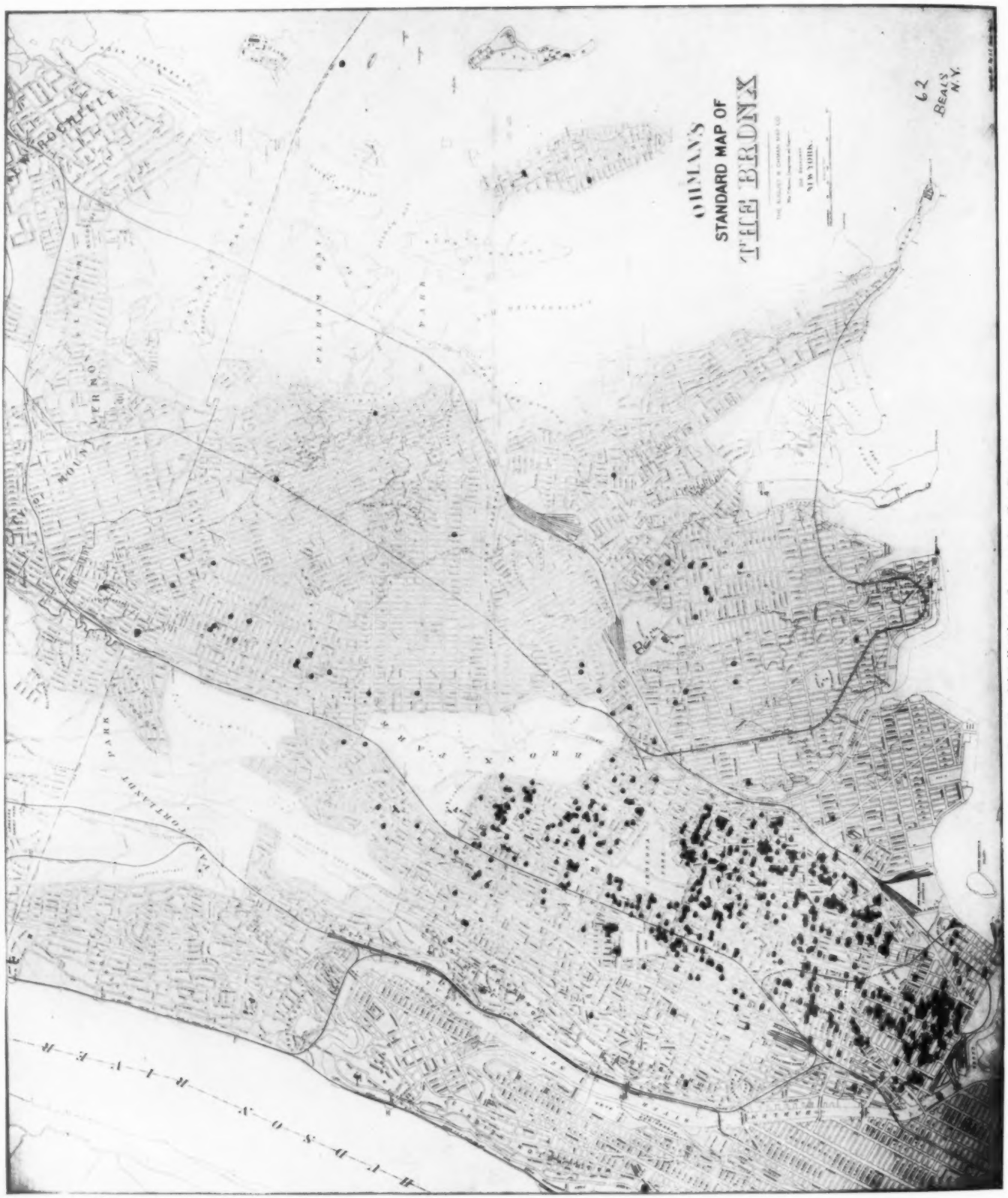

FIG. 3.—Distribution of cases in the Bronx.

FIG. 4.—Distribution of cases in the Borough of Brooklyn.

FIG. 3.—Distribution of cases in the Bronx.

FIG. 5.—Distribution of cases in the Borough of Queens.

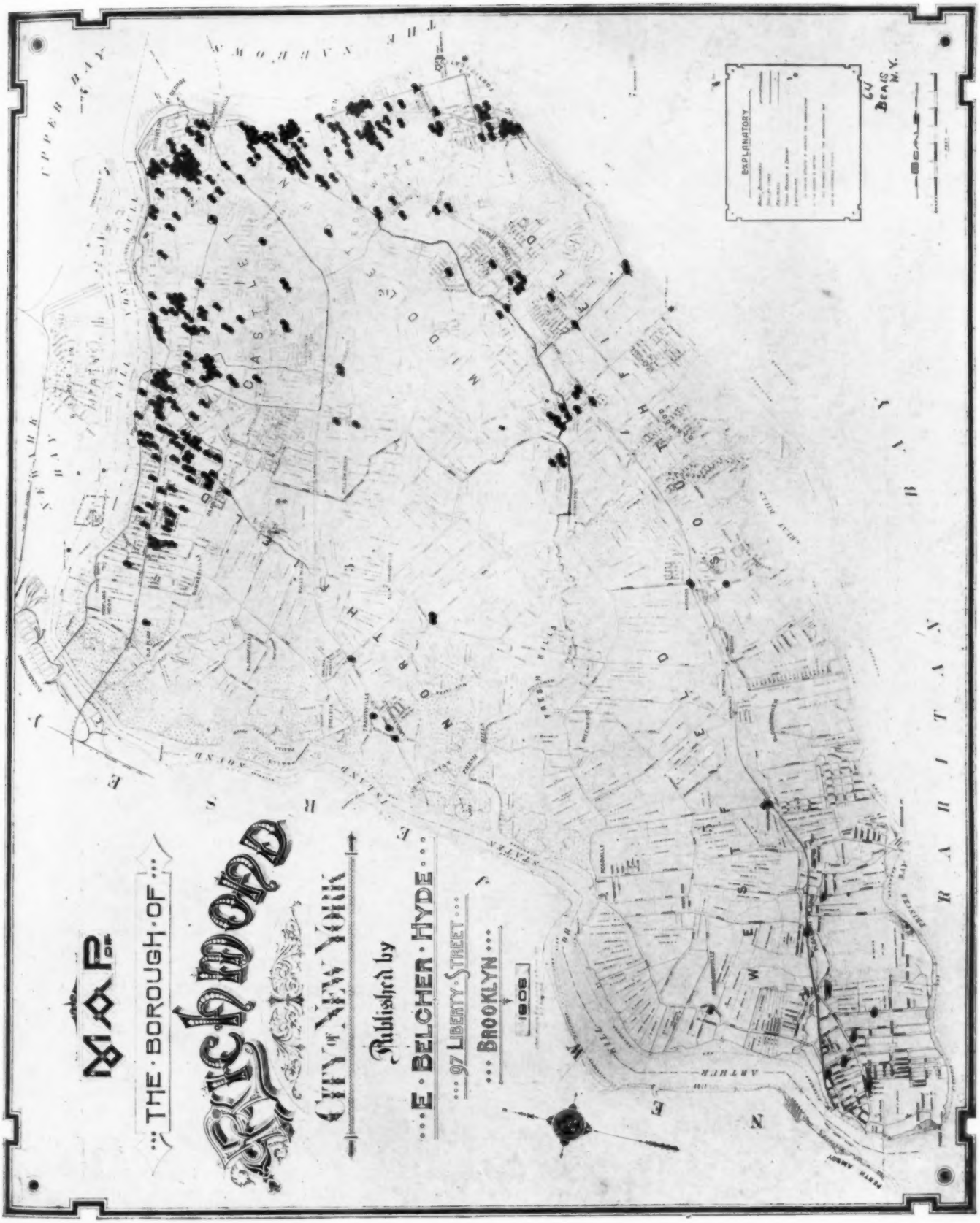

FIG. 6.—Distribution of cases in the Borough of Richmond.

PLACENTAL TRANSMISSION: CREATININE AND CREATINE IN THE WHOLE BLOOD AND PLASMA OF MOTHER AND FETUS.

By E. D. Plass.

(From the Obstetrical Department of The Johns Hopkins University and Hospital.)

The recently developed methods for the quantitative determination of various constituents of normal blood have stimulated the study of the placental transmission of these substances with the hope of deducing some general principles involved in this reciprocal exchange which is so essential to the fetal economy. The relative concentration of a given substance in simultaneously collected samples of maternal and fetal blood should throw some light upon the method of interchange between the two circulations.

The blood is the vehicle by which the materials necessary for growth and repair are supplied to the cells and the waste products removed. The fetus must absorb the former from the maternal blood through the placental villi and may eliminate the latter through the same channel. Nature has endowed the fetal organism with remarkable attributes in order to avoid either a deficit of the essential building materials or a surplus of metabolic products. Clinical and chemical observations show that the growing fetus may store up materials that are badly needed by the maternal organism thus indicating either that the chorionic villi have a certain selective activity whose duty it is to provide the materials necessary for growth and that these pile up in the fetal blood, or that the growing fetal tissues have a greater chemical affinity for these substances and can abstract them from the circulating medium and even lead to a depletion of the maternal stores. The metabolic products that undoubtedly escape from the fetus into the maternal circulation theoretically belong in a different category but likewise must pass outward by simple diffusion or be actively eliminated by the villi.

According to the diffusion theory, the plasmas—the fluids on the two sides of the supposedly permeable membrane—should contain the same amounts of all soluble diffusible substances; whereas, according to the secretory theory, a difference in concentration of certain materials might occur on the two sides of the active membrane when their need was greater in one organism or when their presence was distinctly harmful. The various tissues of the fetus may bear a quantitative relationship to the concentration of a substance in the plasma which is quite different from the relationship existing on the maternal side of the placental barrier. Such a difference has been frequently observed in cases of anemia and osteomalacia where the maternal tissues are literally robbed of iron and calcium in order that fetal development may proceed normally. Such fetal parasitism has furnished the basis for arguments by the advocates of the secretory theory, whereas the underlying factor may well be a difference in affinity without any essential change in the actual transmission of materials. The plasma of the blood in the two circulations should be studied quantitatively by the methods available for the determination of the various anabolic and catabolic materials, in the hope that this problem may be definitely settled.

Our insistence upon the use of plasma or serum values only in support of the diffusion theory of transmission is enforced by the difficulties encountered in the work to be reported on preformed and total creatinine. In the light of known facts it seems best not to consider the whole blood as a unit, as is so frequently done, but to look upon the corpuscular elements as distinct from the plasma. It is quite evident that the contents of the cells do not enter directly into the phenomenon of placental diffusion, but that in these problems the tendency to equalize concentrations must affect primarily the plasma. Many of the reported analyses for the various blood constituents indicate that the composition of the whole blood is quite different in many respects from that of the plasma.

Several chemical studies on placental transmission have recently appeared. Hymanson and Kahn [8] analysed 12 specimens of maternal and fetal blood for the total lipoid content and for the cholestrol fraction, using whole blood for the former determination and serum for the latter. Their figures show no constant variation of either material in any one direction, although the average lipoid content is slightly higher in the fetal blood and the cholestrol somewhat lower than in the maternal. The differences are so slight and so inconstant as scarcely to warrant the conclusion which they draw "that the chorionic villi [seem to] have the function of discriminating which part and how much of each lipoid shall pass into the fetal circulation."

Slemons and Morriss,[9] working with whole blood, determined the total non-protein nitrogen and urea in samples of maternal and fetal bloods collected at the time of delivery and found the same concentrations in both specimens. With no available data concerning the relation between the non-protein nitrogen of the whole blood and of the plasma or serum these figures prove less than they would if it were definitely known that equal concentrations were present in the blood cells and the surrounding plasma. A few scattered published analyses of the urea content of the whole blood and plasma, however, indicate that the concentration of this end-product of metabolism is the same in the cell elements as in the plasma and the figures for whole blood probably hold equally well for the plasma. The work of these authors, therefore, shows quite conclusively that urea passes the placenta by simple diffusion.

The work of Rabinovitch [10] on the amino-acids cannot be advanced as evidence in favor of either theory. No note is made of analyses of simultaneously collected specimens but rather the conclusions are based upon the amino-acid content of the blood which flowed from the two cut ends of the cord. It was found that the blood from the fetal end had a higher

amino-acid value than that from the maternal end, thus indicating, Rabinovitch says, that the blood going from the fetus contains more NH_2-N than that going toward the growing organism. The results as published are very inconclusive and quite contrary to the findings of Morel and Mouriquand as quoted by Slemons and Morriss.

Within the past month, Losee and Van Slyke have published in another connection four sets of determinations of the CO_2-combining power of normal maternal and fetal plasma. The alkali reserve shows no significant variations, the fetus participating equally in the mild acidosis with which the mother is affected.

At the December meeting of the Society of Biological Chemists, Hunter and Campbell,[4] in discussing the distribution of the creatinine and creatine between the corpuscles and plasma of the blood, gave the results of analyses for these two constituents in two sets of fetal and maternal plasmas. The values were the same in the two fluids and were similar to those reported here. These figures are the only ones available for these two materials and indicate that they maintain the same concentration in the two circulations. The work here reported was practically completed at the time the results of these two workers were presented.

In the present work the blood samples were collected as nearly simultaneously as possible and the analyses were begun at the earliest possible moment. The maternal specimens were taken from an arm vein and the fetal from the maternal end of the severed cord or from the distended umbilical vein by means of a needle. Bloods collected at night were preserved on ice until the following morning. When whole blood or plasma was used, coagulation was prevented by the addition of dry powdered potassium oxalate. Most of the analyses were done in duplicate and the color comparisons were always made by two individuals. All the samples were taken from patients who were delivered spontaneously at term. Asphyxiation of the child at birth was noted only once, in Case 13. Obstetrical chloroform anesthesia was usually employed, but in a few cases gas and oxygen were used and in two cases scopolamine-morphine analgesia. The anesthetic used had no influence upon the results. The parity and age of the mother and the duration of labor were likewise tabulated but showed no relation to the analytical findings.

As early as February 1916 a series of comparisons of maternal and fetal blood was begun, Folin's[1] method for creatinine and creatine being used. These earlier analyses (Table I) seemed to indicate that the problem was somewhat complicated. The preformed creatinine values are generally lower than those reported by Folin and Denis[2] for normal adults (1.1-1.4 mgm. per 100 c. c.); but show a close agreement between the maternal and fetal bloods. The total creatinine values are likewise lower than those of Folin and Denis, but the fetal bloods gave consistently higher results than the maternal. The differences in absolute values may possibly be explained by the use of deteriorated standard solutions of creatinine, but the comparisons are obviously not affected by this factor.

In the course of this work it was discovered that by hemolysing the blood before saturating it with picric acid higher values for both fractions were obtained. The greater hematocrit value of fetal blood was already known. A second series of determinations was now made, blood hemolysed by the addition of four volumes of distilled water, as suggested by Myers,[3] being employed. The hematocrit values were obtained

TABLE I.—WHOLE BLOOD—NOT HEMOLYSED.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.		Fetal.	
	Preformed creatinine.	Total creatinine.	Preformed creatinine.	Total creatinine.
1	1.12	3.85	1.75	7.63
2	....	7.92	....	8.73
3	.54	4.19	.72	5.00
4	.90	4.80	.73	6.25
5	.93	4.31	.93	5.68
6	.56	4.68	.69	8.44
7	.62	5.48	.61	5.73
8	.61	4.43	.45	7.02
9	1.26	7.05	1.03	8.60
10	.84	7.05	.96	7.95
11	.80	5.68	.63	6.29
Average	.82	5.40	.85	7.73

by centrifugalizing the undiluted whole blood in 15 c. c. graduated centrifuge tubes for 20 minutes at 3000-3500 revolutions per minute. Satisfactorily pure picric acid was used and the colorimeter readings were corrected by a table similar to that published by Hunter and Campbell.[4]

The results (Table II) in general show less agreement between the two bloods than did the first series. The preformed creatinine varied in an inexplicable manner and,

TABLE II.—WHOLE BLOOD, HEMOLYSED.
(Mgm. Creatinine in 100 c. c.)

Case No.	Maternal.			Fetal.		
	Hematocrit.	Preformed creatinine.	Total creatinine.	Hematocrit.	Preformed creatinine.	Total creatinine.
8		1.12	4.59		1.08	6.72
12	22	3.75	9.55	41	5.24	11.45
13	31	5.29	6.98	41	4.47	8.17
14	30	2.26	5.66	35	2.34	6.18
15	24	1.41	6.00	25	1.87	6.94
16	28	3.37	8.28	35	3.03	10.42
17	25	1.98	8.71	33	3.85	10.72
18	28	1.98	8.33	39	3.00	9.68
19	34	1.55	7.54	34	2.52	9.40
20	33	1.16	6.84	36	2.64	9.50
Average	29	2.39	7.25	35	3.00	8.92

while the total creatinine roughly paralleled the hematocrit values, the relation was so inaccurate that no conclusions could be drawn regarding the comparative concentrations of the two constituents in the bloods.

It seemed that no relationship could be established and that further study would be profitless.* At this time a determination was made upon a sample of human blood plasma by Folin's original method; it was found not only that the total

* More recent observations by another method have indicated that the results for total creatinine in whole blood obtained by the Folin procedure are probably too high and that the variations cannot be taken as conclusive.

creatinine values were much lower but that the development of color in the picric acid filtrate after alkalinization proceeded in a manner similar to that observed in the standard creatinine solutions. This suggested the use of plasma or serum in the study of the problem at hand and offered a new line of attack.

A third series of comparisons was consequently undertaken and a very definite relationship between the two bloods at once became apparent. The Folin method was employed as originally described. The lower total creatinine values make it advisable to make up the 10 c. c. portion of picric acid filtrate after autoclaving to 15 c. c. rather than to 25 c. c. and to read it against a 0.2 mgm. per 100 c. c. creatinine standard. If the serum or plasma shows hemolysis, the results may be disturbed as is shown in Table III. Oxyhemoglobin itself seems to be responsible for only a small part of the additional color development; the addition of small quantities of a solution of crystalline oxyhemoglobin to a standard solution of creatinine produces only a slight accentuation of the color developing after the addition of alkali. The injury to the cells which shows itself by the appearance of hemoglobin in the plasma apparently permits the escape of a reacting substance which disturbs the comparative results.

TABLE III.—DISCORDANT RESULTS WITH PARTIALLY HEMOLYSED PLASMA OR SERUM.
(Mgm. Creatinine in 100 c. c.)

	Maternal.			Fetal.		
Case No.	Hemolysis.	Preformed creatinine.	Total creatinine.	Hemolysis.	Preformed creatinine.	Total creatinine.
9	None	.87	1.85	Slight	.95	2.36
18	Slight	.85	2.14	Moderate	1.15	3.12
19	Marked	.86	3.63	Moderate	.92	2.77
20	None	1.11	1.59	Moderate	1.11	2.10
22	None	1.17	1.81	Moderate	1.15	2.33

The preformed creatinine values are little affected, but the total creatinine figures are considerably disturbed. This points to the presence of some substance which requires conversion by heat before it is able to give the color reaction. Creatine itself is in this category and moreover is in greater concentration in the corpuscles than in the surrounding plasma. In order to determine, if possible, whether the increased color development is due to creatine the following experiment was undertaken: Freshly drawn oxalated human blood was centrifugalized and clear plasma obtained; this was divided into two portions; to one part was added a good trace of cell extract obtained by adding distilled water to the original cell mass; the second portion was preserved clear. Routine Folin determinations were done on both portions and in addition the total creatinine was estimated by the acetic acid precipitation method.[9] The following results were obtained:

	Picric-acid method.		Acetic-acid method.
	Preformed creatinine. (mgm. in 100 c. c.)	Total creatinine. (mgm. in 100 c. c.)	Total creatinine (mgm. in 100 c. c.)
Unhemolysed plasma	1.33	1.98	2.05
Hemolysed plasma	1.35	2.29	2.16

These results, as well as other observations, seem to indicate that most of the added color development which is noted in hemolysed serum or plasma is probably not due to creatine.

Nine pairs of fresh unhemolysed sera were secured and analysed by Folin's method (Table IV). Some difficulty was experienced in obtaining satisfactory specimens because of the great ease with which fetal blood hemolyses.

TABLE IV.—PLASMA OR SERUM.
(Mgm. Creatinine in 100 c. c.)

	Maternal.		Fetal.	
Case No.	Preformed creatinine.	Total creatinine.	Preformed creatinine.	Total creatinine.
4	.78	1.91	.85	1.95
10	.71	1.79	.78	1.95
21	1.38	1.91	1.30	1.93
23	.97	1.68	.96	1.63
24	1.22	1.82	1.07	1.88
25	1.14	1.61	1.14	1.86
26	1.25	1.85	1.03	1.93
27	1.17	1.85	1.14	1.97
28	1.31	2.32	1.33	2.28
Average	1.10	1.86	1.07	1.93

Preformed and total creatinine are present in practically the same concentrations in the maternal and fetal sera and the values obtained are constant within narrow limits. The preformed creatinine is the same as in normal non-pregnant women (1.0-1.2 mgm. per 100 c. c.) but somewhat lower than in normal men (1.3-1.5 mgm. per 100 c. c.). The total creatinine content of all normal human sera seems to be quite fixed (1.6-2.1 mgm. per 100 c. c.). The proportion in which the two components are present is variable, although the total remains the same. This corresponds with the observation that the urinary output of total creatinine is subject to only slight variations, although on occasion a portion of this total may be eliminated as creatine. Women and children are known to excrete creatine and it may be that the presence of this substance in the urine is dependent upon its higher concentration in the plasma.

Summary and Conclusions.—Simultaneously collected samples of maternal and fetal blood were analysed for preformed and total creatinine by Folin's method. The determinations on unhemolysed and hemolysed whole bloods brought out no definite information with regard to the exchange between mother and child, but when serum or plasma was used, a definite relation was clearly established. The concentration of both fractions is the same under normal conditions in the plasmas which are naturally the fluids concerned in the placental interchange.

The use of serum or plasma is essential in the study of placental transmission.

The plasmas of both mother and child contain the same amounts of preformed and total creatinine. The values are the same as those found in non-pregnant women.

The preformed and total creatinine apparently pass between the mother and fetus by simple diffusion.

I wish to express my thanks to the various house officers who have collected the specimens of blood and also to the Depart-

ment of Physiological Chemistry for the facilities and advice which have been given.

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THE OBSTETRICAL SIGNIFICANCE OF THE BLOOD-SUGAR WITH SPECIAL REFERENCE TO THE PLACENTAL INTERCHANGE.

By WILLIAM H. MORRISS.

(From the Department of Obstetrics and Gynecology, Yale Medical School.)

Blood-sugar estimations were begun in this laboratory as part of a plan to study the problem of the placental interchange by systematic comparison of the various constituents of the blood of the mother and her newborn infant. It soon became apparent that analysis of the mother's blood was required not only at the conclusion of labor but also during the periods preceding and following the infant's birth. And finally, observations were made upon pathological cases.

Before the specimen for analysis was secured, the patient had fasted for at least three hours, a period which Hopkins and Graham found sufficient to eliminate errors due to alimentary glycosuria. The analytical method of Lewis and Benedict was adopted; for this has been widely used and has proved to yield consistent results. Since its initial step—dilution of the blood with water—insures thorough hemolysis, the estimation includes the sugar in both corpuscles and plasma. Essentially, the subsequent steps are precipitation of the blood-proteins with picric acid, filtration and, after further addition of picric acid and sodium carbonate to the filtrate, the development of a red color by careful heating. The chemical reaction involved is the reduction of picric to picramic acid by glucose. Comparison of the color obtained with that of a standardized solution of picramic acid determines the amount of sugar in the blood.

In order to control the technique, observations were made upon several individuals with normal carbohydrate metabolism. The results were within the normal limits described by Lewis and Benedict (0.09-0.11%) which are somewhat higher than those obtained by older methods. This fact must be taken into account when my determinations are compared with the results of previous investigators. Probably, the latter are somewhat too low, for the critical studies of McDanell and others have confirmed the accuracy of the Lewis-Benedict method.

BLOOD-SUGAR DURING PREGNANCY.

Until suitable analytical methods were devised, it was supposed that hyperglycæmia existed during pregnancy, or at least during the latter half of this period. The inference seemed to be justified by a number of clinical and experimental considerations. From the respiratory exchange in rabbits, Bohr concluded that glycogen alone supplied the energy required for embryonic development. A similar importance was then attributed to the carbohydrates in the development of the human fetus, and consequently, an increase in the maternal blood-sugar was expected. Furthermore, the susceptibility of pregnant women to alimentary glycosuria, as well as the results when epinephrin was administered, made the suspicion stronger that hyperglycæmia existed. Yet, this is not the case; in uncomplicated pregnancy the blood-sugar is normal. This conclusion, reached by several investigators, is confirmed by my analyses of the blood in 11 patients at various periods of gestation.

BLOOD-SUGAR DURING PREGNANCY.

No.	Age.	Gravida.	Pregnancy.	Glycosuria.	Blood-Sugar. %	Remarks.
1	32	VII	2nd month.	0	0.098	Normal Pregnancy.
2	22	II	3rd "	0	0.119	Twins: aborted at fourth month.
3	21	I	3rd "	0	0.113	Neurotic vomiting, recovery.
4	22	I	6th "	0	0.102	Normal pregnancy.
5	22	II	7th "	0	0.095	Normal pregnancy.
6	22	I	7th "	0	0.107	Normal pregnancy.
7	19	II	7th "	0	0.10	Normal pregnancy.
8	29	I	7th "	0	0.099	Syphilis. Wassermann ++++.
9	25	II	7th "	0	0.149	Very neurotic.
10	26	I	8th "	+	0.095	Mild, transitory glycosuria.
11	21	II	9th "	0	0.116	Normal and near term.

Only in the case (No. 9) of an extremely neurotic woman who was greatly alarmed by the preparations for securing a specimen of blood was hyperglycæmia noted. Normal values obtained in cases of twins, hyperemesis, syphilis, and alimentary glycosuria. Excluding these, the mean value for the blood-sugar in six uncomplicated cases was 0.103% (the extremes were 0.116% and 0.098%). These results agree with the findings of a number of investigators collected in the following table, in which the average is 0.09%.

The significance of a normal blood-sugar during pregnancy becomes clearer if certain facts about the urine are recalled. Spontaneous glycosuria (alimentary) appears in approximately 10% of pregnant women, and glycosuria may be induced during pregnancy much more readily than at other times. Thus, 100 grams of glucose administered to healthy individuals will not provoke glycosuria, but when this amount is ingested during pregnancy, according to Reichenstein, in 37.5% of the cases sugar appears in the urine. Analagous

Summary of Blood-Sugar Determinations in Pregnant Women.

Investigator.	Maximum.	Minimum.	Mean.
	%	%	%
Schirokauer	*0.112	*0.085	.....
Kampf	.....	.....	0.079
Benthin	0.096	0.054	.....
Bergsma	0.136	0.07	0.091
Frank	0.12	0.08	0.095
Neubauer and Novak	0.09	0.05	.....
Jacobson	0.105	0.094	0.098
Morriss	0.116	0.098	0.103

*Plasma.

results have been reported by von Jaksch, Lang, Hofbauer and by Ludwig and Payer; Stolper invariably found sugar in the urine of pregnant women after the administration of 100 gm. of glucose.

Similarly, a small dose of epinephrin causes glycosuria more frequently during pregnancy than at other times. Jäger noted it in 38% of his cases after the administration of 0.5 c. c. of adrenalin; and Christofoletti reports a similar incidence of glycosuria after the administration of 0.3 c. c.

Upon this evidence pregnant women are said to have a low tolerance for sugar; but although clinical experience abundantly supports this conclusion, the explanation is not found in the presence of a hyperglycæmia. Consequently, various other suggestions have been offered. In the predisposition to glycosuria during pregnancy some authorities see the evidence

Blood-Sugar During the Puerperium.

No.	Age.	Para.	Puerperium.	Blood-Sugar.	Remarks.
				%	
1	26	I	1st day.	0.095	Normal Puerperium 7 hours post partum.
2	34	IV	2nd "	0.092	" "
3	19	I	2nd "	0.101	" "
4	23	I	3rd "	0.119	" "
5	22	III	3rd "	0.10	" "
6	28	III	4th "	0.116	" "
7	28	II	5th "	0.118	" "
8	26	IV	5th "	0.118	" "
9	20	I	6th "	0.118	" "
10	24	I	7th "	0.118	" "

of lowered ovarian function, and others the effect of an increase in the adrenal or pituitary secretion. Whatever the relation of the glands of internal secretion to the phenomenon, its immediate cause seems to depend upon the kidneys, which during pregnancy are somewhat more permeable for glucose. Advocates of this view include Novak, Porges, Schirokauer, Mann, Bergsma, and Frank. The last investigator observed glycosuria during pregnancy when the blood-sugar was normal; and in one instance a patient under my care (No. 10) presented a definite but very small amount of glucose in the urine while the blood-sugar was 0.095%. On the other hand, in healthy individuals Hamman and Hirschmann found that sugar appeared in the urine only when the blood-sugar reached 0.17%. At least during the latter part of pregnancy the renal threshold for glucose is low.

In view of the activity of the mammary glands an increase in the blood-sugar was expected during the puerperium but, as in pregnancy, analysis of the blood has shown the incorrectness of confidently held hypotheses. Throughout the puerperium normal values for the blood-sugar are found. Cases selected to represent successive days after the birth present 0.119% as the highest value for the blood-sugar, 0.092% as the lowest and 0.109% as the mean value. Correspondingly, Bergsma found 0.094% as the average in 22 cases. These results indicate an almost identical level for the blood-sugar in the periods before and after the infant's birth. In other words the regulatory mechanism for carbohydrate metabolism in women maintains approximately the same amount of sugar in the blood when a fetus is nourished in the uterus, when an infant is fed at the breast, and when there is no requirement to supply glucose to a dependent organism.

During lactation, it is well known that lactose frequently appears in the urine, and traces of it have also been detected in the blood. When introduced into the circulation, its quantitative elimination by the kidneys indicates that the organism cannot use lactose; and Abderhalden has shown that, except in the digestive tract, there are no enzymes in the body capable of splitting this disaccharide. Therefore, when absorbed from the mammary glands lactose is treated as a foreign body and the kidneys excrete it promptly. Probably in this fact, we have the explanation for the absence of an appreciable increase in the blood carbohydrate during the puerperium.

Maternal Blood-Sugar During Labor.

These studies actually began with determinations of the sugar in the blood of women at the conclusion of the second stage of labor. As soon as the infant was born a sample of its blood was obtained and immediately a sample was also secured from a vein in the mother's forearm. The latter contained a larger amount of sugar than is generally considered normal. At first suspicion was attached to the use of a tourniquet in the technique for obtaining the mother's blood, but it proved unjustified, for identical values obtained whether this appliance was employed or not. Then, it became advisable to learn whether the method of analysis yielded results during pregnancy and the puerperium agreeing with those of previous observers. As normal values were found in both of these periods, analyses were then made during the early part of labor to determine more precisely when the hyperglycæmia appeared.

In 28 normal cases, the mean value for the maternal blood-sugar at the moment of birth was 0.132% (maximum 0.185%, minimum 0.089%). These results are approximately a third

greater than those obtained during pregnancy and the puerperium. For the explanation of the hyperglycæmia several clinical facts pertaining to the conclusion of the birth must be taken into account. Thus, the voluntary muscular effort which expels the fetus, the wrought-up mental state of the parturient woman

MATERNAL AND FETAL BLOOD-SUGAR AT THE MOMENT OF BIRTH.

No.	Age.	Para.	Duration of labor.	Duration 2nd stage.	Maternal glycosuria.	Blood-Sugar. Mother.	Blood-Sugar. Fetus.	Remarks.
						%	%	
1	22	I	11:55	1:35	0	0.143	0.124	Normal labor. Whiffs of chloroform.
2	31	I	27:30	1:10	0	0.135	—	Normal labor. Whiffs of chloroform.
3	20	I	10:15	1:10	0	0.097	0.10	Normal labor. Morphine and tyramine.
4	20	I	19:20	1:05	0	0.161	0.131	Normal labor. Morphine and tyramine.
5	26	I	54:05	3:40	0	0.128	—	Normal labor. Whiffs of chloroform.
6	19	I	18:25	2:20	—	0.137	0.141	Normal labor. Whiffs of ether.
7	19	I	11:45	1:20	—	0.125	0.108	Normal labor. Whiffs of chloroform.
8	26	I	5:10	?	—	0.155	0.112	Prolonged labor, nervous. Whiffs of chloroform.
9	29	I	13:00	0:50	0	0.142	0.106	Normal labor. Whiffs of chloroform.
10	20	I	25:30	1:00	+	0.155	0.124	Normal labor. Whiffs of chloroform.
11	33	II	4:05	1:00	—	0.126	0.11	Normal labor. No anæsthetic.
12	25	II	11:45	0:50	0	0.156	0.124	Normal labor. Whiffs of chloroform.
13	25	II	9:35	2:20	0	0.146	0.108	Normal labor. Whiffs of chloroform.
14	21	II	4:15	0:20	0	0.115	0.103	Normal labor. Whiffs of chloroform.
15	28	II	4:00	1:45	0	0.112	0.086	Normal labor. Whiffs of chloroform.
16	25	II	12:10	1:05	—	0.11	0.075	Normal labor. Whiffs of chloroform.
17	22	II	22:00	2:00	0	0.125	0.101	Normal labor. Whiffs of chloroform.
18	28	III	6:15	1:20	0	0.122	—	Normal labor. No anæsthetic.
19	24	III	6:20	Rapid	0	0.105	0.096	Normal labor. No anæsthetic.
20	22	III	13:30	0:15	0	0.126	0.105	Normal labor. Whiffs of chloroform.
21	36	IV	14:00	0:45	0	0.172	0.122	Normal labor. Whiffs of chloroform.
22	34	IV	4:00	0:50	—	0.124	0.095	Normal labor. Whiffs of chloroform.
23	29	IV	14:20	?	0	0.126	0.094	Normal labor. No anæsthetic.
24	34	V	2:15	?	0	0.123	—	Premature labor. No anæsthetic.
25	30	V	10:45	1:35	0	0.132	0.112	Normal labor. Whiffs of chloroform.
26	31	V	22:00	3:00	0	0.126	0.13	Normal labor. No anæsthetic.
27	23	VI	12:35	0:20	—	0.089	0.06	Normal labor. Whiffs of chloroform.
28	39	VIII	7:00	3:00	—	0.185	0.185	Normal labor. Whiffs of chloroform.

and the anæsthetic administered for the relief of the pain may, singly or together, increase the amount of sugar in the blood. How far each is concerned may not be determined accurately, though the effort has been made to secure evidence bearing upon the problem. However, in the first place, Is an increase in the blood-sugar characteristic of the whole period of parturition?

In five cases the maternal blood-sugar determination at the conclusion of the second stage was compared with another determination made previously, but after labor had begun. The interval between the observations varied from three to twenty-seven and a half hours. In no case did the earlier estimation indicate a hyperglycæmia; the values were practically identical with those during normal pregnancy. For the first stage the average was 0.093% and for the second stage 0.136%. The increase in the blood-sugar, which varies between 30 and 60 per cent, occurs during the latter part of labor and probably is confined to the second stage, the period in which the expulsion of the fetus takes place.

BLOOD-SUGAR VALUES IN THE FIRST AND SECOND STAGES OF LABOR.

Serial Number.	Duration of labor.	Duration 2nd stage.	Blood-Sugar. 1st stage.	Blood-Sugar. 2nd stage.	Blood-Sugar. Difference.	Interval between analyses.	Remarks.
			%	%	%		
26	22:00	3:00	0.098	0.126	0.028	3:00	Normal labor. No anæsthesia.
17	22:00	2:00	0.088	0.125	0.037	3:30	Normal labor. Whiffs of chloroform.
16	12:10	1:05	0.081	0.11	0.029	6:30	Normal labor. Whiffs of chloroform.
30	16:00	4:00	0.105	0.164	0.059	15:45	Mid-forceps operation. Complete anæsthesia.
10	27:30	1:00	0.094	0.155	0.061	27:30	Normal labor. Whiffs of chloroform.

Certainly, if an anæsthetic was employed, its influence was one factor in the causation of hyperglycæmia. In most instances, as soon as the head reached the perineum, whiffs of chloroform were administered simultaneously with the uterine contractions; and after vulval dilatation began the analgesia was deepened to anæsthesia. The whole period of chloroform administration was half an hour or less, and the amount of the drug used was rarely more than two or three drachms.

Anæsthesia induced either with chloroform or ether causes hyperglycæmia. Heinberg found from 0.3 to 0.6% of blood-sugar associated with chloroform poisoning. With lighter anæsthesia, smaller amounts were observed but even under these circumstances Hersch and Reinbach found hyperglycæmia. Similarly, the first hour of ether anæsthesia is attended with a rise of 5 to 26% in the blood-sugar (McGingen and Rois), and if prolonged, there is a further rise representing from 32 to 89% (Epstein and Aschner). In general these findings are confirmed by my observations upon dogs, which add a noteworthy fact, namely, that with chloroform narcosis the maximal blood-sugar is attained during the early part of the anæsthesia.

For example, in one instance the blood-sugar estimations were as follows:

Control: Before the anæsthetic was started.. 0.154%
Half an hour after the anæsthetic was started. 0.252%
One hour after the anæsthetic was started.... 0.247%
Two hours after the anæsthetic was started.. 0.245%

If comparison is made between the analytical results when the patients were given chloroform and when they were not, we find further proof of the influence of the anæsthetic. In

six cases delivered without an anæsthetic the average blood-sugar was 0.122%, whereas the corresponding average for those who were given chloroform was 0.137%. Nevertheless, if an anæsthetic is not employed, a rise in blood-sugar occurs at the conclusion of labor and is illustrated by Case 26, in which the first analysis yielded 0.098% and that at the end of the second stage 0.126%. This increase, we believe, must be attributed to the voluntary muscular effort used in the expulsion period. The influence of the uterine contractions, which of course are involuntary, must be small or entirely absent, for the blood-sugar generally remains low during the time when cervical dilatation is in progress.

It is pertinent that in the study of the relation between muscular work and the sugar-content of the blood uniform results have not been obtained. Liefman and Stern and also von Moraczewski found that muscular effort caused an increase in blood-sugar, but Wieland found it decreased from 0.09% (normal) to 0.065%. In dogs, stimulating the muscle with the faradic current, Reasch found that in eight instances the blood-sugar rose, in four it fell, and once there was no change.

Indirect evidence such as my observations afford indicates that voluntary muscular effort during labor increases the blood-sugar. Thus, in the case of primiparous women, in whom the expulsive stage is relatively longer and the requisite effort relatively greater, the mean value for the blood-sugar was 0.138%; in multiparous women the corresponding average was 0.129%. Although the highest blood-sugar observed, 0.185% (Case 28), occurred in an 8-para it was associated with prolonged, severe expulsive pains and, consequently, chloroform was administered more generously than usual.

When the cases are grouped according to the duration of labor, the findings point toward a definite relationship between the voluntary muscular work and the percentage of sugar in the blood. In eight cases in which labor continued less than seven hours the mean value for the blood-sugar was 0.123%, whereas in 20 cases with the labor lasting a longer time the mean value was 0.136%. Nevertheless, the blood-sugar does not always vary with the length of labor, for a higher value obtained in a case continuing five hours (No. 9) than in one continuing 54 hours (No. 5). More frequently, it seems that the determining factor is the length of the second stage, and this also is a more accurate measure of the voluntary muscular effort. Thus, the average blood-sugar, when the explusive period lasted half-an-hour, was 0.108%, when it lasted from one to one-and-a-half-hours, 0.135%, and when it lasted two and one-half to three hours, 0.144%.

What part of the rise in blood-sugar should be attributed to emotional causes, it is impossible to estimate; but we are inclined to believe it is very small. Even when patients were excited and almost uncontrolable the blood-sugar has not been higher than in the case of multiparous women, whose previous labors had terminated successfully and who, therefore, in the present labor were relieved of serious concern.

At the conclusion of obstetrical operations, as would be expected, high values for the maternal blood-sugar are found, for generally to the effect of prolonged and vigorous muscular effort is added the influence of an anæsthetic. Some idea of the rise in blood-sugar is given by the analytical results in a case of forceps (No. 30), in which in the first stage of labor there was 0.105% blood-sugar and at the time of the birth 0.164%. But the difference between these analyses is not

BLOOD-SUGAR IN ABNORMAL CASES.

No.	Age.	Para.	Duration of labor.	Maternal glycosuria.	Blood-Sugar. Mother.	Blood-Sugar. Fetus.	Remarks.
					OBSTETRICAL OPERATIONS.		
					%	%	
29	23	I	20:45	0	0.14	0.132	Low forceps. Chloroform. Normal infant.
30	30	VII	16:00	0	0.164	0.123	Mid-forceps. Chloroform. Normal infant.
31	24	I	.....	0	0.116	0.113	Mid-forceps. Chloroform. Normal infant.
32	34	IV	62:00	0	—	0.136	Breech extraction. Chloroform. Stillborn infant.
33	35	V	8:50	—	0.125	0.119	Version. Ether anæsthesia. Stillborn infant.
34	36	II	.....	0	0.163	—	Vaginal hysterotomy. Eclampsia. Chloroform.
35	38	I	.....	0	0.285	—	Cæsarean section. Chloroform. Pre-eclamptic toxæmia.
					TOXÆMIA OF PREGNANCY AND ECLAMPSIA.		
36	25	I	11:20	0	0.082	—	Albuminuria. Normal labor. Chloroform. Normal infant.
37	26	I	5:30	0	0.105	—	Albuminuria. Normal labor. Normal infant.
38	23	I	10:40	0	0.139	—	Albuminuria. Observation six hours post partum.
39	42	IX	.....	0	0.221	0.058	Nephritic tox. Prem. separation of placenta. Stillbirth.
40	34	II	.....	0	0.097	—	Eclampsia. Ante partum. 1 convulsion.
41	36	II	.....	0	0.128	—	Eclampsia. Ante partum. Observation after 3 convulsions.
42	21	I	.....	0	a) 0.151 b) 0.183	—	Eclampsia. Intra partum. 1 convulsion: a) before, b) after.
43	18	I	.....	0	0.136	.....	Eclampsia. Post partum. 12 convulsions.
44	33	IV	.....	0	0.256	.....	Eclampsia. Post partum. 3 convulsions.
					OTHER ABNORMALITIES.		
45	36	I	12:10	0	0.191	0.133	Imbecile mother. Normal labor. Chloroform. Premature infant.
46	23	I	17:15	0	0.215	—	Profound anæmia. Hb. 50%. Chloroform. Normal labor.
47	25	IV	48:00	0	0.082	—	Syphilis (Wassermann ++++) Normal labor. Infant alive.
48	24	I	11:55	0	0.144	0.127	Mitral stenosis and insufficiency. Chloroform. Normal infant.
49	20	I	3:00	0	0.113	0.092	Glycosuria during pregnancy. Chloroform. Normal infant.
50	21	I	17:40	0	0.159	0.168	Prolonged administration of nitrous oxide. Normal infant.
51	34	VII	3:40	0	0.143	a) 0.099 b) 0.096	Twins. (Double-ovum.) Normal infants at term. Chloroform.

greater than may obtain in normal cases with chloroform anæsthesia. On the other hand, practically a normal blood-sugar may exist after half-an-hour of complete anæsthesia (No. 31), and although unusual, this result resembles others obtained on normal cases (Nos. 14, 15, 16, 27). As in these instances no determinations for blood-sugar were made during the first stage, it is impossible to say whether a rise occurred

in the second stage, but in any case it was not sufficient to cause hyperglycæmia.

The hyperglycæmia in Case 35—an elderly primipara threatened with eclampsia—is attributable to the influence of the anæsthetic, for the operation was performed before the onset of labor and pre-eclamptic toxæmia causes no disturbance in carbohydrate metabolism (Nos. 36 and 37). Even with convulsions, provided the determination is not made immediately after an eclamptic seizure, the blood-sugar may be normal (No. 40). It is true, nevertheless, that prompt analysis after a seizure reveals a notable increase in blood-sugar. Upon one occasion in the study of an eclamptic patient, a specimen of blood was obtained shortly before a convulsion occurred and another just after the seizure. In the former the sugar was 0.151% and in the latter, 0.183%. For this rise the convulsion was responsible, but it is uncertain whether the muscular contractions or the nervous mechanism governing carbohydrate metabolism was the basic factor. Neubauer found that the blood-sugar curve in nephritic patients ran parallel with that of the blood pressure, and saw in this relationship the evidence of stimulation of the higher nerve centers. Similarly, hyperglycæmia associated with uræmia and with apoplexy, according to Weiland, is of central origin. Without denying such a possibility, my observations show that high arterial tension is not always accompanied by hyperglycæmia, for Case 37 with a blood-pressure of 205 mm. of mercury presented 0.105% blood-sugar.

The blood-sugar appears to reach a higher level in nephritic toxæmia than is common in eclampsia, though my observations have been too few for generalization. Thus, a patient (No. 39) whose clinical history warranted the diagnosis of nephritis presented 0.221% blood-sugar, whereas in five eclamptics the corresponding figures were 0.097%, 0.128%, 0.136%, 0.151% and 0.256%. All of these patients recovered and were discharged with the urine free from albumin. But there may be a relationship between the character of the acute renal injury and the level of the blood-sugar; and, if so, the more severe the damage to the kidney, the higher the blood-sugar. Benthin, too, found a low blood-sugar in eclampsia and gives as the extremes in nine cases 0.041% and 0.159%. Consequently, he believes that the underlying pathological changes in eclampsia have very little, if any, effect upon the blood-sugar, though convulsions, high arterial tension, and cerebral lesions may cause notable hyperglycæmia. This view, endorsed also by Bergsma is supported by my observations.

The Fetal Blood-Sugar and the Placental Interchange.

The fetal blood was obtained from the placental end of the severed cord. Duplicate analyses upon specimens so obtained and upon others aspirated from the umbilical vein yielded identical results. As it was evident that with either procedure the blood came from the umbilical vein, the simpler method of collecting the sample was adopted. Having just left the placenta on its way back to the fetus this blood was arterial. The structure of the umbilical arteries and their prompt contraction after the infant is born rendered unsuccessful the efforts to secure a sample of the blood passing from the fetus to the placenta. Comparison of the arterial and venous blood in the umbilical cord of dog-embryos showed a difference in sugar content, though only a small one and not beyond the limits of experimental error.

In 24 normal cases the mean value for the sugar in fetal blood was 0.115% (extremes 0.185% and 0.06%). Two-thirds of the analytical results were within the limits normal for adults, and the remaining cases presented slightly higher values. When the mother, under anæsthesia, was delivered by an operative procedure, the average for the fetal blood-sugar was 0.125%, a finding which suggests that generally an increase in the maternal blood-sugar is accompanied by a rise in the fetal. On the other hand, when the mother was not given an anæsthetic, the average fetal blood-sugar was 0.11%.

Two infants born prematurely at the 7th month presented 0.062% and 0.08% blood-sugar respectively. In three cases the blood of still-born infants at term yielded 0.058%, 0.119% and 0.135%. From these data, it appears, there is nothing characteristic in the percentage of blood-sugar in still-born infants.

Analyses of the blood of healthy new-born infants, comparable with those included in my normal series, have been recorded by Bergsma, who found 0.1065% the mean value in six cases, a figure not unlike my average in 24 cases. Older infants are said to present normal values (Bass, Mogwitz, Goetsky, Bing and Widelow), though Cobleiner found hyperglycæmia in late infancy.

From my analyses it appears that there is slightly more sugar in the maternal blood than in the fetal—a fact intimated by the averages 0.135% for the mother, 0.115% for the fetus, and borne out when the cases are studied individually. In 19 normal cases, the maternal values were higher; and in five they were practically identical with the fetal. The mean difference was 0.027% in favor of the maternal blood.

This difference, it seemed possible, was explained by the fact that the maternal sample was taken from a peripheral vessel. And to learn if this were true, animal experimentation was resorted to. In a non-pregnant dog under ether anæsthesia samples of blood were secured from the femoral vein and from the vena cava about the level of the uterine veins. The sugar-content of the former was 0.209% and of the latter 0.215%. These are equivalent analytical results. For our purpose, however, the results of a more crucial experiment are important.

In the case of a pregnant dog near term, under ether anæsthesia, laparotomy was performed and samples of blood were secured from a uterine vein and from the umbilical vein of the most accessible embryo. There was 0.139% blood-sugar in the maternal and 0.123% in the fetal blood. Obviously, these results duplicate the clinical observations upon women at the conclusion of labor and demonstrate that there is less sugar in the fetal blood than in the maternal when the latter is obtained from a uterine vein.

While the requisite conditions attending animal experimentation make it impossible to rule out the effects of the anæsthetic, this was accomplished clinically in several normal cases,

the patients declining to take an anæsthetic, (Nos. 11, 19, 23, 26). In three instances slightly more sugar was found in the maternal blood; in the fourth practically equal amounts were present in the two circulations. Hence it appears that, even when anæsthesia is not employed, the maternal blood is richer in sugar than the fetal blood, though the difference becomes greater when chloroform, ether, or nitrous oxide is administered.

From the results of his observations in six cases, Bergsma concluded that the sugar-content of the blood in mother and fetus is the same. But his work is open to criticism, for the specimens were not obtained simultaneously—between them at times there was an interval of twenty minutes. And as the maternal specimen was the last to be secured, the normal value found may merely indicate the rapidity with which the value for the blood-sugar falls at the end of the second stage.

With regard to the mechanism responsible for the passage of glucose from mother to fetus, comparison of the sugar content of the two circulations lends no support to the hypothesis requiring the action of an enzyme. This doctrine advocated by Hofbauer rests chiefly upon his demonstration of glycolytic ferments in glycerine extracts of the placenta. Their function, it may well be, is the preparation of glycogen, stored in the placenta, for passage to the fetus; but, as I have said, the results of blood analysis certainly do not indicate that they or other enzymes effect the transmission of glucose through the organ. Indeed, they rather speak against it. Thus, in a case of double-ovum twins, where each fetus acquired its food-stuffs through a separate placenta, the blood-sugar of one was 0.099% and of the other 0.096%. It is difficult to imagine such equality if an enzyme action is responsible for the transmission of the glucose, whereas equality would be expected if diffusion is responsible.

In animals* with hyperglycæmia, artificially induced, Cohnstein and Zuntz proved that glucose passed through the placenta in accord with the laws of diffusion. The data in my series of cases indicate that this process also accounts for the transmission of glucose to the human fetus.

Fetal and Maternal Blood-Sugar.

(In cases where two observations were made upon the mother.)

First stage.	Second stage.	Fetal.	Remarks.
%	%	%	
0.094	0.155	0.124	Normal labor. Chloroform.
0.081	0.11	0.075	" " "
0.088	0.125	0.101	" " "
0.098	0.126	0.13	" " No anæsthetic.
0.105	0.164	0.123	Mid-forceps. Complete anæsthesia.

If the determinations upon the fetal blood are compared with those upon maternal blood during the early part of labor, the latter with one exception are the lower. On the other hand, at the moment of birth the maternal values are generally somewhat higher than the fetal; occasionally the same values obtain in both organisms. Probably, as the concentration of sugar increases in the maternal blood, that in the fetal blood also rises. With diffusion the responsible mechanism for the placental transmission, this result would be expected. Furthermore, the difference, noted both clinically and experimentally between maternal and fetal values, is in full accord with a diffusion process; the higher maternal concentration insures the flow of glucose toward the fetus.

As normal values appear in pregnant women the maintenance of a suitable amount of carbohydrate in the fetal circulation does not depend upon a maternal hyperglycæmia Consequently, if diffusion is the process responsible for a suitable supply of glucose to the fetus, relatively lower sugar values would be expected in the fetal blood. Such are actually found. At the conclusion of labor the concentration of glucose in the fetal blood is approximately 12% lower than in the maternal blood.

These findings suggest a prompt disposal of glucose on the part of the fetus, which may depend either upon rapid oxidation or upon unusual facilities for storage. To some extent the first possibility is discredited by the results of my experiments to determine the relative rapidity of glycolysis in the two circulations. When samples of maternal and fetal blood were placed in a thermostat at 38° C. and determinations made from time to time, it appeared that the sugar decreased in both at the same rate. Similar experiments will be made, corresponding organs of the adult and the new-born infant being employed. But in any event probably a great facility for storage of carbohydrate in the fetus is an important factor in maintaining its level of blood-sugar relatively lower than the mother's.

Conclusions.

1. Normal blood-sugar values (0.09-0.11%) prevail during pregnancy and the puerperium.

2. During the early part of labor the values are normal, but in the second stage the blood-sugar is increased. In 28 cases at the moment of birth the average maternal blood-sugar was 0.132%.

3. The rise in the blood-sugar is partly due to the mother's voluntary afforts to expel the fetus, and it is accentuated by the use of an anæsthetic.

4. At the moment of birth the fetal blood-sugar is lower than the maternal. In 24 normal cases, in most of which an anæsthetic was used, the average fetal value was 0.115%.

5. The concentration of glucose in the two circulations is such that the placental interchange may readily be explained by the process of diffusion; and the lower concentration in the fetal blood assures a flow of glucose from mother to fetus.

6. After obstetrical operations higher values are found for the blood-sugar in both mother and fetus, and are explained by the influence of the anæsthetic.

7. Normal blood-sugar values prevail in pre-eclamptic toxæmia though a rise occurs just after a convulsion. Also after repeated convulsions or with pronounced renal involvement the percentage of blood-sugar may be notably increased.

* For these experiments guinea-pigs and a cat were used; a solution of glucose was introduced intravenously.

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CHANGES IN THE BLOOD PICTURE AFTER NUCLEIC ACID INJECTIONS.

By Clarence A. Neymann, M. D.

(From the Laboratory of Internal Medicine, Henry Phipps Psychiatric Clinic, The Johns Hopkins Hospital.)

During the last decade many workers [1] have reported, some favorably and others unfavorably, concerning the therapeutic action of nucleic acid in those diseases which theoretically ought to be influenced by an increase of the leucocytes. It is not the purpose of this report to discuss this issue, but rather to direct the reader's attention towards some changes in the blood picture which we believe ought not to be neglected, especially when repeated injections of nucleic acid are given.

Schittenhelm and Bendix,[2] using the rabbit as an experimental animal, found that nucleic acid in itself was not very toxic and that it was very slow to be absorbed. When it was injected subcutaneously or intramuscularly, indurations resulted. Intravenous injections, except in minute quantities, caused acute nephritis.

As we had the treatment of patients in view primarily, the use of intravenous method of application was precluded. We also employed rabbits in our first test work, using the sodium salt of nucleic acid, and adding to this sodium cinnamate, arsenic, and quassia, according to the formula originated by Lundvall,[3] and recently recommended for the treatment of

dementia præcox by Bayard Holmes.[4] The mixture is made according to the following prescription, which from now on we shall refer to as Lundvall's solution:

Quassini depurati sicci	2.0
Aquæ destillatæ bullientis, q. s. ut fiat	50.0
Boil in a water bath for one and a half hours, filter, and add	
Hetoli (*i. e.*, sodii cinnamati)	1.0
Sodii nucleinati	10.0
Acidi arsenosi (in solution)	0.005
Boil until all is dissolved, filter, and add	
Aquæ destillatæ bullientis, q. s. ut fiat	50.0

This solution, which contains the two strongest known agents for producing leucocytosis, namely sodium nucleinate and hetol, together with arsenic and quassia, was injected into the thighs of four healthy rabbits. The temperature of these animals had been taken, the leucocytes and the erythrocytes had been counted, and the hæmoglobin had been determined daily for a week previous to the experiments. All of them showed practically no fluctuation of these four factors previous to the injection of 1 c. c. of Lundvall's solution. Then the animals gave evidence of extreme pain. This was especially noted during and directly following the injection. The temperature first fell, then gradually rose about one degree above normal, during the first sixteen hours after injection. The number of erythrocytes and leucocytes and the percentage of hæmoglobin fell twenty-four hours after the injection. The red blood corpuscles decreased about a million, the white about two thousand and the hæmoglobin five to ten per cent. Forty-eight hours after the injection the red count had again reached the normal height, but it took the animals a week to recover their normal percentage of hæmoglobin. The white count, in which we were especially interested, rose perceptibly above normal in only two animals. In one an increase of six thousand lasted two days, in the other an increase of from three to four thousand lasted nine days. These results were not encouraging, but thinking that the fault might lie in the lack of absorption due to the induration at the point of injection, we next experimented with cats, carnivorous animals, which we thought might give a different reaction.

Four cats were consequently injected with 1 c. c. of the solution; their weight, averaging 2.5 kilograms, was about equal to the average weight of the rabbits. Their reactions, as regards pain and temperature, were not different from those of the latter animal. The red count and the percentage of hæmoglobin showed less tendency to drop, and in the two cases in which there was a slight drop the animals recovered rapidly within twenty-four hours. The maximal leucocytosis occurred three days after injection. There was an average increase of eleven thousand leucocytes. In one case an increase of eighteen thousand was recorded. These increases lasted about eight days, declining step-like from day to day, as can best be seen on curve No. 1, a fair example of the curves obtained.

A second injection of 1 c. c. of Lundvall's solution, after the count had come down to normal, gave a slight increase of the leucocytes in one animal; this leucocytosis of from two to three thousand lasted a week. A second injection of 2 c. c. of the solution, in another animal gave no increase at all (Curve No. 1).

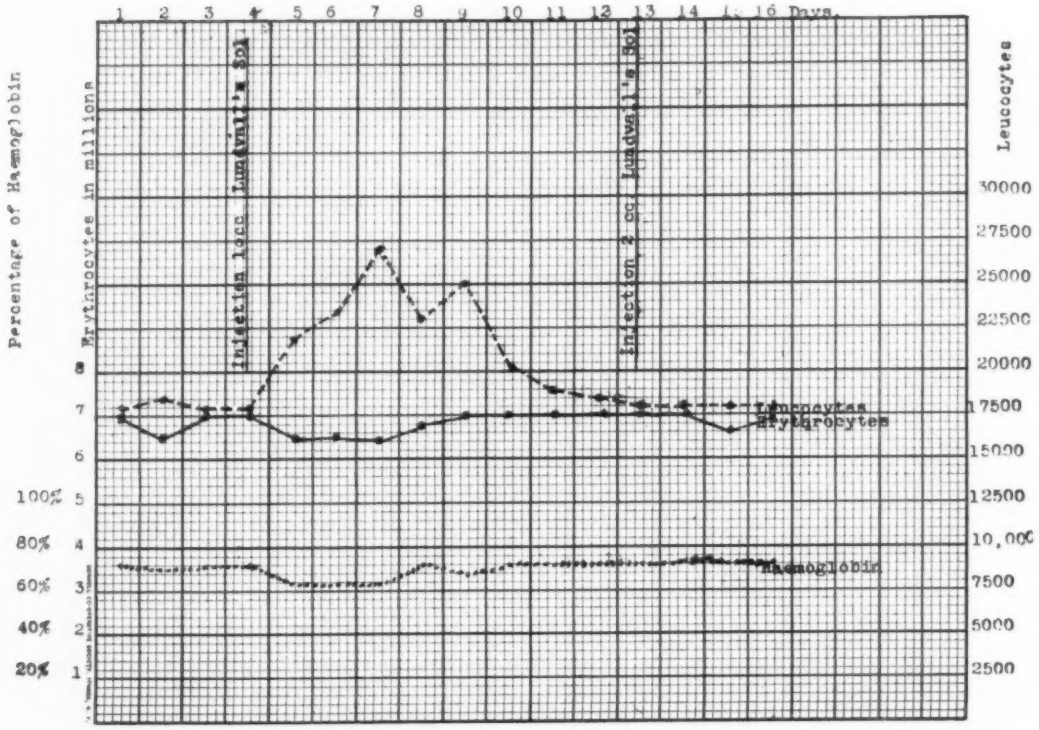
Differential counts (Curve No. 2) showed a relative increase of the polymorphs and eosinophiles compared to the small and large mononuclears. No pathological elements were observed. Busse[5] called attention to this relative increase of leucocytes over lymphocytes in patients treated with nucleic acid alone; Landerer,[6] working with hetol, demonstrated an eosinophilia in his patients.

Having thus gained some experience with the action of the solution, we next decided to apply it to the treatment of patients. We selected four patients, one of whom, Mr. S., represented a depressive paranoid reaction type; one Miss T., a hysterical reaction type with schizophrenic features; one, Miss Z., an undoubted schizophrenic reaction type, and the last, Miss F., a depressive reaction type with marked schizophrenic features.

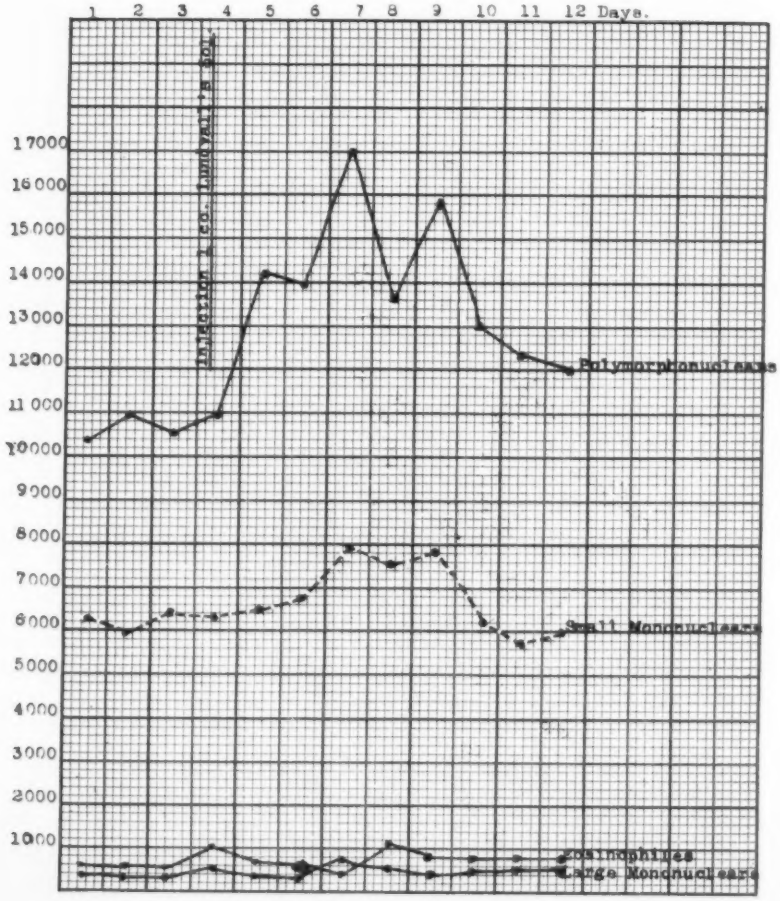
Curves Nos. 3, 4, 5 and 6 will best illustrate the results obtained in regard to leucocytosis, percentage of hæmoglobin, and the number of erythrocytes. Three main facts stand out: The comparatively short time that the leucocytosis lasts, the gradual increase in doses necessary to produce leucocytosis as the patient develops a tolerance for the drugs, and the decrease in the percentage of hæmoglobin and in the number of erythrocytes. The hæmoglobin curve was not plotted in the case of Mr. S. (Curve No. 3). In this case, also, the hæmoglobin decreased from 95 per cent before the treatments were begun to 85 per cent after the last treatment. The decrease in the percentage of hæmoglobin became truly alarming in the cases of Miss T. and Miss Z. (Curves Nos. 4 and 5) reaching as low as 65 per cent in both cases. We were indeed glad to see these patients regain normal blood pictures after the injections of Lundvall's solution had been stopped and iron and arsenic administered in their stead. The differential counts showed the relative increase of polymorphs and the eosinophiles mentioned above. No pathological elements were observed.

As to the psychic behavior of the patients, we can best characterize it as similar to that which one would expect after any shock. The injections are very painful. The rise in temperature of from two to three degrees causes a feeling of being ill at ease, with headache and nausea as accompanying factors, and the whole procedure, necessarily carried on in spite of the protests of the patient, is a cause for excitement. As a result of this shock the patients transfer their attention to the difficulties caused by the treatment and place their own internal difficulties more in the background. Thus, the three schizophrenics who showed a catatonic tendency, were more inclined to talk, and were generally brighter during the twenty-four hours directly following a treatment, whereas Mr. S. the depression case, whose worries were centered on the imaginary prospect of being put in jail and castrated, now worried about the time of the next treatment.

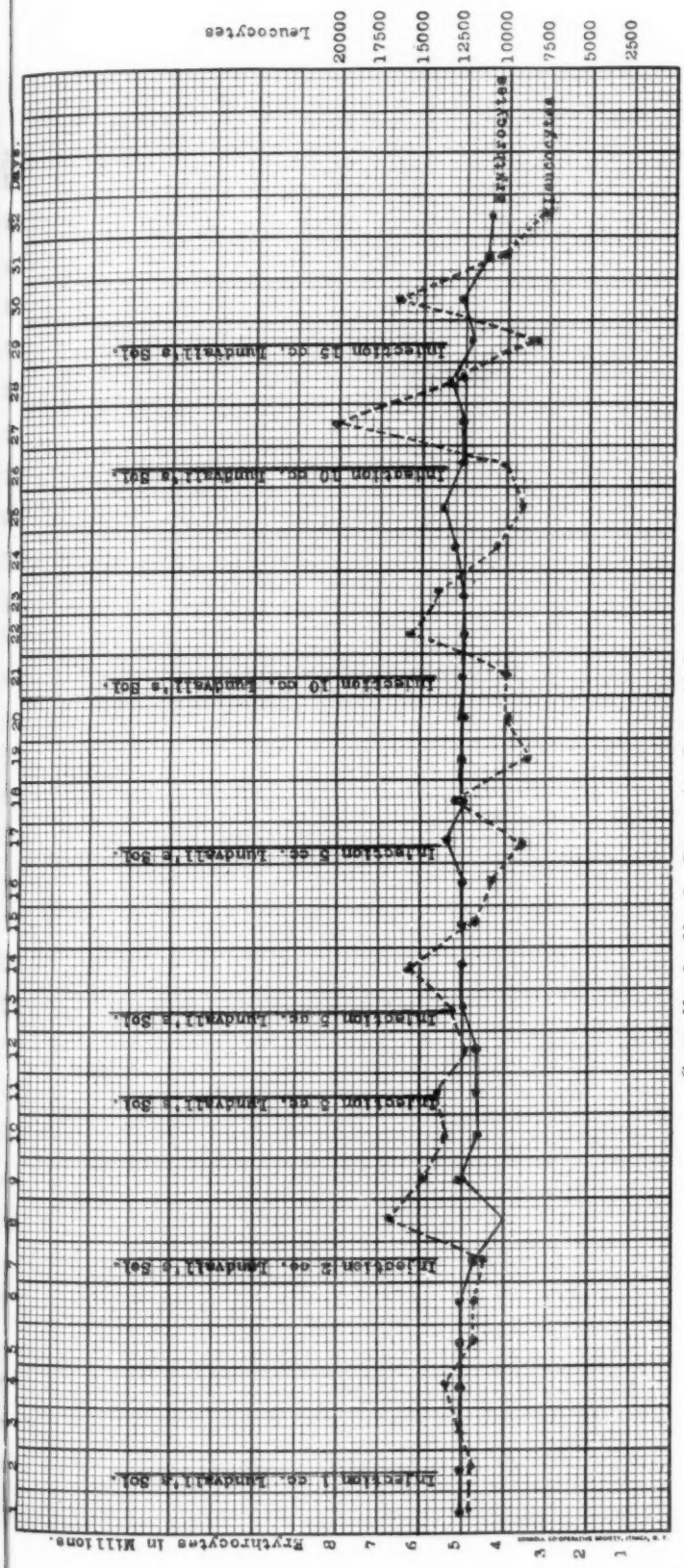
On account of the marked decrease in the percentage of hæmoglobin in two of our patients and the less marked though



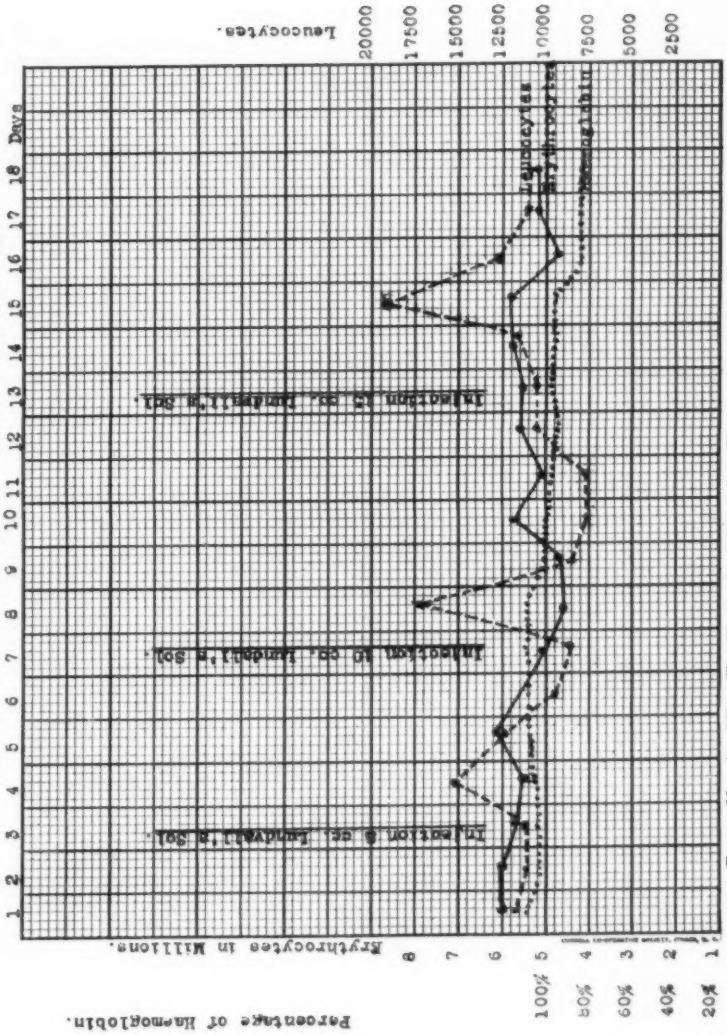
Curve No. 1.—Cat. Weight 3200 Gm.



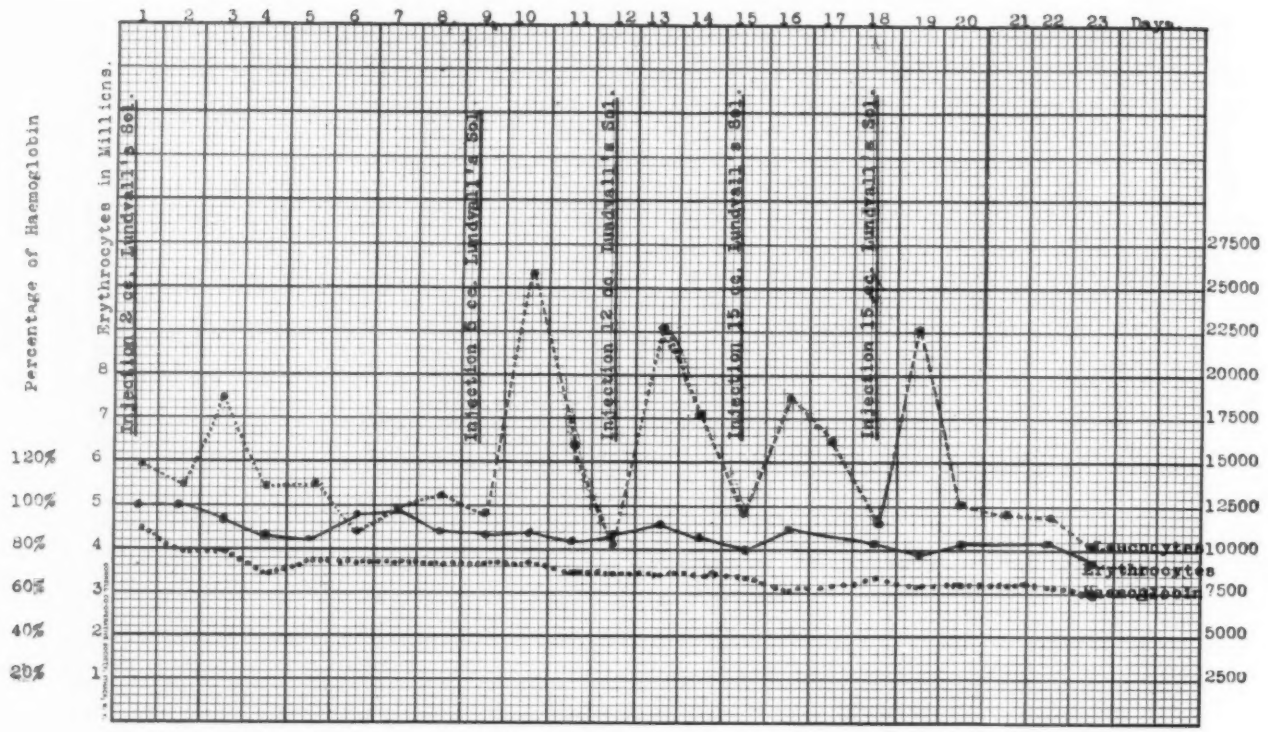
Curve No. 2.—Cat. Weight 3200 Gm.



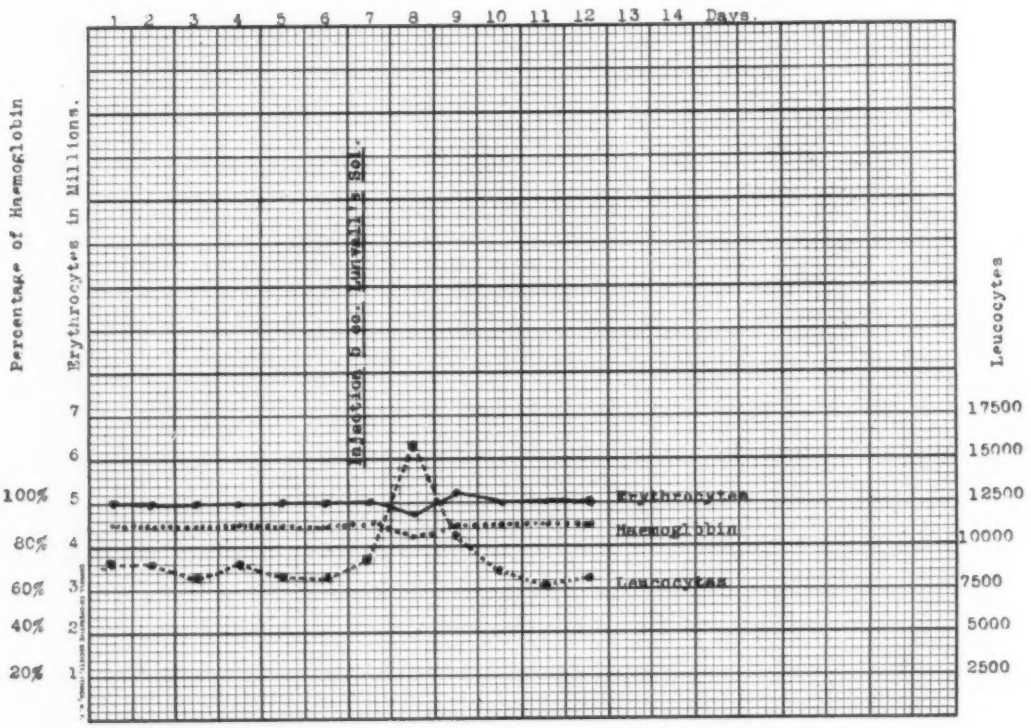
Curve No. 3.—Mr. S. Depressive Paranoid Reaction Type.



Curve No. 4.—Miss T. Hysterical Reaction Type with Schizophrenic Features.



CURVE No. 5.—Miss Z. Schizophrenic Reaction Type.



CURVE No. 6.—Miss F. Depressive Reaction Type with Schizophrenic Features.

apparent decrease of this substance in the other two, and in all our experimental animals, we did not feel justified in continuing the treatments. Though the patients quickly regain their original number of erythrocytes, it takes several weeks for the percentage of hæmoglobin to reach the normal figure. These disadvantages would in themselves seem to preclude the continued regular injection of the solution.

SUMMARY.

1. The injection of Lundvall's solution causes an increase in the number of leucocytes.
2. This leucocytosis lasts from one to two days.
3. The patient develops a tolerance for the solution.
4. The hæmoglobin decreases alarmingly if the treatments are repeated at close intervals.

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1. A good summary of the work done can be found in Merck's Annual Report, 1913, XXVII, 1.
2. Deutsche med. Wchnschr., 1904, XXX, 227.
3. Hygiea, 1907 LXIX, 1142: Tidsskrift for Nordisk Retsmedicin oz Psykiatri, 1910, X, 227. Lundvall: Sonderbroschure, Christiania, 1912.
4. Bayard Holmes: The Insanity of Youth and Other Essays, Cincinnati, 1915, pp. 19 and 195.
5. Busse: Arch. für Gynäk., 1906, LXXXV, 1.
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LEUKEMIA, PSEUDOLEUKEMIA AND HODGKIN'S DISEASE.*

By C. H. BUNTING, M. D., Madison, Wis.,
AND
J. L. YATES, M. D., Milwaukee, Wis.

The diseases which have as their most prominent feature a progressive enlargement of the lymph nodes form a group which offers many difficulties in differential diagnosis. These difficulties beset not only the clinician but also the pathologist. In fact, it may be said that, if the ordinary form of glandular tuberculosis be excluded, there is left a group of diseases which have so many common factors that separation into its component members is only a matter of opinion. This has led to a variety of attempts at classification with results acceptable, as a rule, only to the originators.

The common factors in these diseases, as we have observed them, are in brief as follows:

1. The presence (or history) of a primary focal inflammatory lesion, usually but not necessarily in the upper part of the digestive or of the respiratory tract (teeth, tonsils, adenoid tissue, sinuses, bronchi).
2. Progressive enlargement of the lymph nodes, with or without accessory extranodal tumors.
3. Chronic course, with late moderate secondary anæmia and with the constant development of a fever usually of an irregularly intermittent character, exceptionally of the Murchison type.
4. Eventual fatal termination within a relatively brief period of years (2-5).
5. The occurrence during the course of the disease of either the blood picture described by Bunting[1] as the primary blood picture of Hodgkin's disease, or of a leukemic blood picture.
6. The occurrence of a primary lesion in the germinal centers leading to an early loss of architecture in the lymph nodes through an extensive proliferation of diverse cells but with common factors in the picture.
7. The constant occurrence in the lesions (nodal and extranodal) of organisms of the diphtheroid type.

The group possessing these common features includes the diseases ordinarily designated as Hodgkin's disease (lymphogranulomatosis), leukemia of the lymphatic type, pseudoleukemia, lymphosarcoma, malignant lymphoma, chloroma, leukosarcoma, etc., showing a nomenclature as varied as the classifications. One's first reaction after coming in contact with various members of the group is to wonder whether the same effort that has been applied to the separation of the members of the group, if it had been applied in an attempt to bring them together, would not have increased our understanding of them. In other words, are not their resemblances greater than their differences?

In general the blood picture is held sufficient to separate one group of these cases as specific diseases under the name, "leukemia." This does not seem to us justifiable. The evidence from our series of cases, even though they be few, seems to indicate that the leukemic blood picture is an incidental feature in the course of the disease, or rather an individual reaction to a stimulus which in another case may fail to produce the same reaction. It seems impossible to tell clinically whether or not a patient has a leukemic blood picture. Pseudoleukemia and leukemia are indistinguishable without a blood examination. This was apparent to us in a case recently published in which the cultural findings[2] were emphasized—a case apparently the counterpart of that published by Wende.[3] With all the clinical signs of leukemia, the patient showed the Hodgkin's blood picture until his departure from observation during the last weeks of his life. Owing to this departure we are unable to say whether, as in Wende's case, a terminal leukemic picture was developed.

* A paper presented before the Association of Am. Physicians, May, 1916.

[1] Bull. Johns Hopkins Hosp., 1914, XXV, 173.

[2] Bunting and Yates: Bull. Johns Hopkins Hosp., 1915, XXVI, 376.

[3] Amer. Jour. Med. Sci., 1901, CXXII, 836.

In three cases of so-called pseudoleukemia we have seen the Hodgkin's blood picture persisting for months and in one case for years. In a fourth case, seen by the courtesy of Dr. Warfield at the Milwaukee County Hospital, the Hodgkin's blood picture was succeeded before the patient's death by the picture of acute lymphoblastic leukemia.

The occurrence of a leukemic picture in Hodgkin's disease is apparently relatively rare. However, in one case sufficiently under our control so that all data necessary for accurate diagnosis were obtainable, there occurred a change of the blood picture from the secondary polymorphonuclear leukocytosis of the intense type of the disease to a leukemic picture. With a count of 72,000 leukocytes 65 per cent were of the mononuclear type, both large and small, but atypical and immature. Some of the cells showed mitotic figures. The occurrence in the blood-smear of megalokaryocytes suggested that this represented a bone-marrow reaction. The picture later reverted to its original type shortly before the death of the patient, who showed at the post-mortem examination the lesions of acute Hodgkin's disease. In two other cases diagnosed clinically as Hodgkin's disease (and in one confirmed by the excision of a gland) there appeared in blood-smears submitted to us the formula of chronic lymphocytic leukemia but without apparent marked leukocytosis. We have observed also in a monkey, inoculated with diphtheroid bacilli, the occurrence of a similar picture (99 per cent lymphocytic forms, 1 per cent polymorphonuclear) without any apparent increase in the number of the leukocytes. In another human case, one of acute lymphoblastic (or possibly myeloblastic) leukemia, we have seen the picture of acute leukemia develop through the Hodgkin's blood picture.

Moreover, we find that it is equally as difficult to tell, from the pathological study of the lymph glands in this group of diseases, whether or not the patient had a leukemic blood picture. The glands in a case of malignant lymphoma are identical in appearance with those in chronic lymphocytic leukemia. There is no difference between the infiltrations in the large-celled acute leukemic picture and those in lymphosarcoma or pseudoleukemia. In each case one finds, with an increase in size, a loss of glandular architecture and a diffuse infiltration with the type of cells chiefly involved. It is with such observations in mind that the leukemic blood picture seems to us of incidental importance in the disease in which it occurs.

Pathological study of the glands in these cases shows, as we have just suggested, that in each there is a progressive increase in size, with early loss of architecture. The increase in size is due to a general proliferation of cells which show to a certain extent diverse types. Recognizing the common factors we may, nevertheless, make three broad groupings of the cases even at the risk of earning the censure passed on others who have attempted to classify the group.

In the first class, that of Hodgkin's disease proper, one recognizes a lesion in which destruction of lymphocytes is dominant, but in which proliferation of fibroblasts and of the reticulo-endothelial cells is prominent. This proliferation is atypical, leading to giant-cell formation. One may recognize three terminal pictures in this group.

1. Almost complete sclerosis (typical fibroblastic proliferation).

2. Sarcomatoid picture (atypical fibroblastic proliferation).

3. Endotheliomatoid picture (atypical endothelial proliferation, usually with marked giant-cell formation).

The last two have the local histological picture of malignancy but without invasion (or only slight) and without any tendency to metastasis or recurrence.

In the second main group of cases we find a large-celled proliferation infiltrating the whole gland. This apparently begins with a marked proliferation of the large cells of the germinal centers, a proliferation which is atypical and which fails also to show the differentiation into lymphocytes. In very early cases there may be a thin collar of lymphocytes about these extremely large germinal centers. In cases slightly later, there are architectural indications of very large germinal centers but no lymphocytes, and ultimately there is a general infiltration of the gland with these large cells and obliteration of the normal architecture. There may be some fibroblastic proliferation, and giant cells may be found. From the character of the predominant cell this might be termed the lymphoblastic group.

In the third group there is a diffuse proliferation of the small lymphocyte with very early loss of architectural landmarks. Scattered lymphoblasts and atypical endothelioid cells may occur. This may be spoken of as the lymphocytic group.

While we make thus pathological distinctions between broad groups, they are not always clear-cut. The fibroblastic proliferation and giant-cell formation may be so marked in the latter groups that a transition picture toward that of Hodgkin's disease is seen. In fact we have no desire to separate the groups but rather would consider them as representing a varied reaction to the same or to similar stimuli. Were it not for the rapid course of acute leukemia (both myeloblastic and lymphoblastic) we should be inclined to see in these cases examples of the general pathological law, that a toxin stimulates in mild doses (lymphoblastic and lymphocytic groups) but in strong doses destroys (Hodgkin's disease).

The above discussion embodies the conclusions at which we had arrived even before we had found that with careful technique diphtheroid organisms could be obtained from the glands in all of these conditions. This finding has been very abundantly confirmed by the work of others. There seems to be no question as to the constant occurrence of the organisms, but only a question as to the significance to be attached to their presence in the lesions. The majority of investigators have concluded that the organisms occurs in too diverse conditions to be of etiological importance.

While we can ask only for a Scotch verdict at the present time, evidence which points toward their etiological significance from our experience is in outline as follows:

1. The constant occurrence of the organisms in Hodgkin's disease and in the allied group under discussion. This is true not only for single determinations but for repeated examina-

tions, as, for example, seven successful cultures from one case over a period of five years (neck, groin and axilla).

2. The occurrence of the organism where it would explain the lesion. We may cite, as examples, its occurrence, as reported, in the cutaneous nodules in a case of acute pseudo-leukemia; and the occurrence of the diphtheroid as the only stainable organism below the surface and distributed in mucosa and submucosa in two cases of primary intestinal Hodgkin's disease.

3. The occurrence of the so-called Hodgkin's blood picture in the whole group of cases enumerated, in laboratory animals (monkey, rabbit) inoculated with the living organism, and in one normal individual inoculated with the dead organisms (vaccine).

4. The occurrence of abcesses in laboratory animals (monkey, dog, rabbit, guinea-pig, horse) at the portal of inoculation with lymph-gland changes similar to those seen in early Hodgkin's disease.

5. The occurrence of complement deviation by the use of the patient's serum and diphtheroid organisms (unpublished series of experiments by Yates and Kristjanson).

6. The occurrence of a glandular reaction and of a skin reaction in patients injected with immune serum resulting from the use of a diphtheroid antigen.

Such evidence we believe would be accepted as indicating etiological significance for almost any organism except members of the diphtheroid group. It is accepted for organisms almost as widely distributed as the diphtheroids. We must admit that the final test, the production of a disease in animals comparable to the human type, has not been accomplished. The attempt to produce a chronic disease in animals less susceptible than man (in whom the virulence is not great in the majority of cases) has resulted usually in lowering the resistance of the animal to organisms more acutely fatal. However, even here death has not occurred before the regional lymph glands have developed definite changes similar to those shown early in the group of diseases under discussion.

This question, however, must apparently be temporarily unanswered without, however, disturbing in the main our contention as to the general relationship of the diseases discussed.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

NOVEMBER 6, 1916.

The Recent Epidemic of Infantile Paralysis. DR. HAVEN EMERSON, New York City.

See article in this number.

NOVEMBER 20, 1916.

1. Exhibition of Patient With a Calcified Cyst in the Right Pleural Cavity. DR. G. J. HEUER.

The patient, a colored man fifty-three years of age, entered the hospital in the service of Dr. Janeway, October 12, 1916. He complained of cough, shortness of breath and pain in the right side. In his past history the only points of interest are the occurrence of typhoid fever and of pneumonia thirty-two years ago. The pneumonia, he states, was upon the left side. His first wife died of tuberculosis at the age of thirty-eight.

Present Illness.—Four weeks before admission to the hospital, while lifting a 300-pound sack of fertilizer, the patient had a sudden severe pain in the right side, accompanied by cough and shortness of breath. The symptoms were so marked that he was compelled to stop work, but was able to walk to a doctor's office. The physician advised him to remain in bed. During four weeks in bed the pain has persisted unchanged. The cough has continued.

Physical Examination.—The physical signs were those of fluid at the right base, which was thought to be purulent in character. A needle was inserted into the chest, but met with firm resistance. No attempt was made to insert the needle farther, and no fluid was obtained.

X-rays of the patient's chest showed a remarkable condition. In the right side of the thorax was a clearly defined shadow, roughly pyramidal in shape, the apex directed upward, the base resting in part upon the diaphragm. This shadow measured 13 cm. in vertical height, was 10 cm. wide. An X-ray taken with the patient in an upright position showed this cystic structure to contain fluid which presented a definite level about 3 cm. from the very tip of the mass. The clearly defined wall of the structure measured 5 mm. in thickness. The mesial surface of the mass was in contact with the mediastinum. The lateral surface came almost to the rib margin.

Sputum examination was constantly negative for tubercle bacilli. It was purulent in character and contained large numbers of cholesterin crystals, pus cells, and epithelial cells. The amount of sputum varied, some mornings amounting to a cupful.

The temperature was slightly elevated, rising to 99° and 100° during the day. The leucocytes were 7000, the red cells, 3,500,000, hemoglobin, 60 per cent. The polymorphonuclear cells were not increased. There was no eosinophilia. The Wassermann test was negative.

A positive diagnosis could not be made. Various possibilities, such as calcified dermoid cyst, echinococcus cyst, an old circumscribed empyema associated with calcification, and a localized hematoma associated with calcification, were considered.

Operation.—About twelve inches of the ninth rib were resected, and later, about six inches of the eighth rib. The parietal pleura was stripped from the chest wall. Palpation of the pleura showed directly underneath it a hard, bony mass, the limits of which could not at first be determined. On incising the parietal pleura, what appeared to be the bony wall of the structure was found densely adherent to it. The dense adhesions were cut, and the enucleation of the calcified mass begun. It was found that over the entire anterolateral surface of the mass there were these dense adhesions between it and the pleura. The flattened surface of the mass in contact with the diaphragm was much less adherent and could be readily separated from this structure. The deeper surface of the mass was in contact with the concave surface of the lower lobe of the lung; it was not at all adherent and could be readily separated from it. The mesial aspect of the mass was densely adherent along the anterior mediastinum. During the course of the removal of the tumor, the cyst wall along its mediastinal border was entered. There was an escape of a thin, yellowish, purulent material, and some bubbles of air. At the upper lateral border of the mass, where the calcareous wall apparently had not been penetrated, there was again an escape of

fluid and air bubbles, and it was assumed that here there was a communication between the cyst cavity and the lung. The entire mass was finally removed without hemorrhage, without, indeed, tying a single blood vessel. It was noted after the removal of the tumor that the visceral pleura of the concave lower surface of the lung was not thickened. The large cavity left after the removal of the mass was drained with a single rubber tube.

There were no post-operative complications. The patient is well two months after operation.

Examination of Specimen.—The calcareous wall is complete, with the exception of one area along the mesial aspect of the tumor, where the mass was densely adherent to the mediastinum. The wall varies from 2 to 5 mm. in thickness. At the time of removal, the interior of the shell was lined with a putty-like dirty brown deposit, which could easily be scraped off from the wall of the cyst. This material on examination showed nothing excepting cellular detritus. The cyst contents were very thoroughly studied by Dr. Guthrie, without anything being found to establish the nature of the cyst. Sections of the cyst wall showed calcified tissue. In no place was true bone found.

2. Medical Problems of the War. DR. W. H. WELCH. (Abstract.)

There would not be time to attempt the treatment of any such broad subject as the title would indicate. What I shall have to say will relate to some of the medical problems of the war, and more particularly to my own personal experiences. That necessitates saying a few words as to the circumstances of my making the trip to England and France last August and September.

I went over primarily to make some inquiries and observations which I thought might be helpful in planning and organizing the new School of Hygiene and Public Health which is to be established here. I wanted to talk over some of our problems, but it was very difficult to arrest the attention of anybody over there on anything except the problem of the war. I was also interested in the qualifications of certain young men for taking up some of the work here. It soon became perfectly apparent that no one is coming over here while the war is on. In the first place it is difficult to get hold of them, and they were so intensely absorbed in their work it was difficult to divert their attention. I soon made up my mind that any men willing to come here while the war is on would doubtless be the type of men we would not want. Their duty is there with their country.

The second purpose of the trip related to a commission that the President of the United States has placed upon the National Academy of Science, and I was accompanied by Mr. George Hale, the eminent astronomer, who is head of the solar observatory at Mt. Wilson, California, which is supported by the Carnegie Institution. He has been engaged since last March in undertaking this work for the organization of the scientific resources of the country in questions of national security and national defence. It is obvious to anyone that it would be most helpful to learn what they are doing on the other side in those directions stimulated by the war. The opportunity of meeting members of the government and eminent scientific men was intensely interesting, but that is a subject by itself, although it occupied a considerable part of our time.

When I went over I did not plan to go to France, and did not suppose that I should have the opportunity of seeing very much of the actual medical and surgical work. Fortunately, I had had France included in my passport, so it was possible to go there. I might say here that I was not aware of the importance of taking with one all the credentials one should have. I went in rather a casual way with an ordinary passport, and gave our embassy both in London and Paris a very unnecessary amount of trouble, which would have been avoided had I taken letters from our ambassador and others.

One should not think of going over there simply because he wants to go to see things. One must have a serious purpose before going. Indeed, one is not likely to get a passport unless he has a serious errand, and unless he has, he should not be there. In a way it is almost like going to a house of mourning without being called by a purpose.

We left the United States on the 5th of August and went over on an American steamer, landing at Liverpool. I came back on an English boat, the *Baltic*, and the contrast was interesting. Apparently, everyone wishes to go on the American boats on account of the security. On that boat everything was done to make our presence widely known. We advertised ourselves all the way across. An American flag was painted on the outside of the boat, which was brightly illuminated at night. We went up like a banner of flame through the Irish Channel. That is, of course, a matter of safeguard. Coming back, on the other hand, everything was done to conceal our presence. There were no lights at all and the decks were perfectly dark at night. We did not know where we were. There was no record posted of our daily run, nor of the latitude or longitude. The course that we took was not known, except perhaps to the captain of the boat whose orders were handed to him at Liverpool.

On landing we went to London where we had our headquarters, making several side trips, especially to Oxford, where I went three times to see Dr. Osler. I also went to Cambridge and a few other places. We crossed the Channel at the end of August from Southampton to Havre, and visited Paris. Although the trip to France was hurried, lasting only about two weeks, we had rather exceptional opportunities for seeing things in Paris, in the American hospital at Neuilly, at Compiègne, etc. When it was time to go back, we found we were held up in Paris on account of a sudden taking off of the boats crossing the Channel. Mr. Hale took a French boat home from Bordeaux. I remained nearly a week longer before the boats started again from Havre to Southampton.

On the whole I think I saw about as much as one could see in that short space of time. I owe that very largely to Dr. Osler. I would like to say in passing that both Sir William and Lady Osler were really very well and very active indeed in work of all sorts relating to the war. I thought Dr. Osler was in extremely good form, intensely interesting and interested, and a very great influence over there. He has done important things of real national service to us over here, particularly those of the medical profession. For some reason or other it was a long time before we had any medical men over there observing the military medicine and surgery. Why, I do not know, but they were not there. Dr. Osler interested himself and wrote to the President here and to others, and through his interest and activities it was arranged that a group of very excellent young doctors from our Army and Navy Medical Corps should go over to take advantage of the opportunities for important observation. Dr. Osler introduced me to Sir Alfred Keogh, the Director General of the Army Medical Corps and head of all things medical, who opened the way everywhere, both in Great Britain and France, and afforded me exceptional opportunities of seeing things and of meeting men I desired to meet. When Dr. Carrel heard I was in Paris he spent nearly two days there while the Minister of War was making arrangements for me to go to his hospital. Everything requires time and there are many formalities. Things are not quickly attended to.

Now a few words on some of the broad aspects. In the first place the conditions under which the warfare is conducted are perfectly unparalleled. Of course, there is a large experience from past wars of military surgery, hygiene and organization of hospitals, etc. This is valuable and all important. I do not think that they utilize sufficiently some of the experiences in our Civil War, but the problems are to a large extent novel because the conditions are new. If you read of military surgery, you will note it is based largely upon the assumption that in warfare bullets from small

caliber guns fired with great velocity are to be used; whereas, in the present war the wounds are terribly lacerated and often contain broken shrapnel. One shell may burst into thousands of fragments raining down upon the men. You can imagine what novel conditions result from that. Poisonous gas, too, is a terrible thing which was never heard of before. Warfare in the trenches is new also, and there the men are subjected to new conditions of infection. I heard a most vivid description of the environment of the soldiers in the front line trenches from Dr. John McCrae, who is over there in a Canadian hospital. He told of the shells shrieking with no let up by day or night, the shrapnel bursting into these myriads of fragments and the killed and wounded everywhere. No wonder there are effects upon the personality and nervous system which are absolutely new and which one has had no experience with before.

Again, by way of a general statement, we are in possession of weapons of defense which have not been tried on any such a scale before against the diseases and wounds of the war. Here was an opportunity to test the value of our inoculations against typhoid, paratyphoid, cholera, dysentery and tetanus. It is a wonderful chance to see what these new discoveries are worth and to try them out. There has also been a great opportunity in sanitary matters and the possibility of having pure water, new methods of incineration, etc., and the sanitation of camps, which has not been in the possession of military men before. Broadly stated, there are certain things which stand out with great prominence in regard to sanitation and preventive medicine in this war. The diseases which have been so devastating in past wars are to a large extent controlled. This is probably the first war where the soldiers have died to a greater extent from wounds inflicted by bullets and shells than from disease. The control of disease is one of the great lessons of the war. Typhoid and paratyphoid *a* and *b* were not unknown in the earlier part of the war, but are now controlled by vaccination with killed cultures of the bacilli. Typhoid and paratyphoid vaccines are given in one dose, one vaccine, and I believe that on the Eastern front, where there was some cholera, they included the cholera vaccine at the same time. I believe it is possible to use the Shiga bacillus in one vaccine with the germs of a great variety of diseases. When we recall the terrible mortality from typhoid fever in our Spanish-American War, you can see what a tremendous gain this is.

Equally significant is the control of tetanus. Early in the war, when there was not enough serum, it was obvious that there was going to be a great deal of tetanus. It is now practically under control.

Cerebrospinal fever is quite satisfactorily treated at present. Their results at first were very unsatisfactory, when it was found that they were using a practically inert antimeningitic serum both in Great Britain and France. They had not known it and the treatment of Dr. Flexner threatened to become discredited. He obtained some of the serum to test and it was found to be worthless, which has led to the examination of not a few of the commercial antimeningitic sera. The armies are now being supplied with a really good serum, largely through the agency of the Rockefeller Institute, and the results are extremely satisfactory.

In the East they have had diseases which have not prevailed much in the West. Dysentery has occurred on the Western front, but has prevailed chiefly in the East.

Just a word about tuberculosis, which is one of the medical problems of the war. The situation as regards that disease is really a very serious one in France. It does not appear to be so in England, and probably is not in Germany. We do not, of course, have any information as to what the situation may be there. In France there is a frightful amount of tuberculosis among the soldiers. To a very large extent, those who have been temporarily disabled are found to be tuberculous. It raises the question as to what the explanation may be. Probably tuberculosis is more common in France than in Great Britain or Germany, so there are larger numbers of soldiers with latent tuberculosis. In the second place, it is probable that not sufficient care was taken in the examination of the recruits, so as to exclude those with active and especially open tuberculosis. Then, too, France has been behind the other countries in the tuberculosis movement, and they have not had the lessons in protection, especially the importance of the open air life.

I might say that in general the soldier's life is a healthy one. Take the British Tommies, for example. The British workingmen and clerks have been trained into admirable soldiers, and you would hardly recognize them as the class that some have represented as a rather degenerate type. No praise is too high for the British soldier. The men are healthier than they were before and probably tuberculosis, instead of being on the increase, is controlled. This is not so, however, among the French. It is a really serious and urgent problem, which is causing great concern over there.

The results obtained by the surgeons are most remarkable. I feel that important contributions have been made, and are being made, toward the treatment of wounds. The use of the X-ray is, of course, of incalculable advantage. This is obviously the case when you consider the rôle the lodgment of foreign bodies in wounds must play.

A word as to the sanitation of camps. I regret that I did not personally visit one of the camps near the front. Sir Alfred Keogh was anxious for me to go and had arranged for it, but I had to hurry back and so missed the opportunity. I made up for it to some extent in London when I returned and went to see the field experiments which are being made. That is something which is not shown very generally, I think; at least our doctors over there in connection with the embassies had not seen these places. I was taken to a large open field, fenced all around, and there it was most interesting to see the experiments they are making in such matters as purification of water, latrines, disposal of waste, etc. I was most enthusiastic about the incinerators. There is no expense for fuel, as they are going day and night. All waste is dumped there and burned up.

As regards the organization of the hospitals, of course in England they are all the so-called base hospitals of different types. The general organization is this. When a soldier is wounded in the trenches, he may have to wait until dark before he can be safely removed, so that he may have to have first aid there. He is then carried back from the trench to the hospital at the front, where he is looked after more thoroughly and is perhaps operated upon. He may stay there several days if necessary, but the treatment is usually temporary, and he is sent back from this front hospital to the casualty clearing station, where his destination—whether he shall be sent to a base or a semi-base hospital—is determined. There he also may remain and be treated a third time, if he is an emergency case. He is then sent to Paris or to the Versailles region, or if he is in British territory, to one of the hospitals around Boulogne. The distribution to the individual hospital is determined by distributing officers. The active operating centers are not, strictly speaking, the base hospitals. The American Ambulance controls about 2000 beds, but less than 600 are in the actual operating center. Where Dr. Blake is (Hospital No. 76 in the Versailles region) they have 250 beds in the active hospital, which occupies a large school building and is very well adapted to the purpose. From there the patients are moved on as soon as they can be to the outlying dependent hospitals or convalescent homes. The experiences of the individual hospitals may be very different according to the class they belong to. Thus, we have the casualty clearing station with one kind of experience, and then the semi-base hospitals that see a different class of wounds or diseases; and still more different the patients in England, who have been carried across the Channel to genuine base

hospitals, which are quite different from the hospitals nearer the front. Then there are hospitals of various special sorts. A very great problem, to which they are already beginning to turn their attention, is the future of the disabled soldier. You can imagine what a tremendous problem that is. They are beginning to establish institutions for the industrial training of these men. Such is the work that Miss Winifred Holt has been doing for the blind in Paris.

The first friend I met after my arrival in London was Dr. Adami, who is in London in charge of very important statistical work, looking after the records of the Canadian soldiers. A great deal is done to make sure that the records are available for statistical study and analysis, and for the history of the war later. The British Army has a very excellent statistician, who is in charge of it all. After the war they will have the benefit of all that systematic work as regards history taking, etc. Dr. Osler appeared the next morning and said that was his day for visiting the heart hospital at West Hampstead. He visits different hospitals at different times. They have established special hospitals for the observation of different classes of disease or injuries. This one was for the reception of patients with the so-called "soldier's heart." At the Maudesley Hospital all the cases of neurasthenia, and especially the shell shock cases, are received. This is no new thing, but is one of the contributions of our Civil War. One of the best things done in our Civil War was the establishment of these special hospitals, especially that notable one in Philadelphia for nervous injuries, to which Drs. Keen and Weir Mitchell were sent, and where Weir Mitchell did that memorable work that turned his attention to the field of neurasthenic disorders. The working up of heart cases is another contribution of our Civil War, particularly of Dr. Da Costa—that particular group of cases where there is insufficiency of the heart attributed to the terrible strain of forced marches, etc. The cases in the West Hampstead Hospital are in that group. You can imagine how interesting it is to have the opportunity of studying them by the newer methods, the electrocardiograph, etc. Perhaps some of you have seen some of the discussions about it. There was one before the Royal Society of Medicine by Mackenzie. If so, you know, more or less, the points of view. Perhaps the most important point is that the majority of these cases apparently give a history of damage to the heart before they were enlisted. They have a history of rheumatism, or breathlessness on going up stairs or on exertion. In other words, they did not have perfectly normal hearts and they could not stand any really great physical strain. In fact, some think these terms are misnomers, and that it is merely the fact that the condition under which they live has unmasked the disorder which was already there. That is probably taking an extreme view.

Another hospital I visited with Dr. Osler was the Canadian Hospital at Cliveden. We motored over one beautiful day from Oxford to that charming place where Major Astor lives and where they have had this fine hospital constructed. It is of the barrack type of military construction, which again is a contribution from our Civil War. This used to be called the American system of hospital construction. I did not know of it until I went to Germany the first time, when I saw a hospital at Leipzig which they called "built on the American system," and I found that it was on the barrack plan of construction. At Cliveden various classes of patients are received, both the wounded and patients with diseases. There I first visited a ward given up to patients with the so-called trench nephritis. The word "trench" is applied to all sorts of disorders and diseases which are not clear as to their causation. It is often a misnomer, as the conditions occur in men who have not been inside the trenches, but you hear of trench fever, of trench foot, of trench shin, trench nephritis, etc. This nephritis was first recognized as a disease occurring in camps among the soldiers in our Civil War. Dr. Osler spoke to me about it and said it was quite well described as one of the camp diseases, so it is not new. There is a great deal of interest attaching to it. I saw one ward practically filled with patients with albuminuria, dropsy and other evidence of unmistakable nephritis. The question as to the etiology is open and there are various views held. I came across from the other side with Dr. Hugh Cabot, who has been in charge of the Harvard Hospital. He was much interested in this group of cases. He had found the streptococcus in the urine in somewhat similar cases in this country. I might say that a great deal of interest attaches to these streptococcic infections. They told me that the viridans group plays a considerable part, and that by making systematic examinations of the blood, using considerable amounts of blood, the streptococcus is found in surprising frequency and in the most varied groups of cases. This is, of course, interesting and one of the medical problems of the war.

I referred to the Maudesley Hospital, which was not open before the war. This hospital is entirely for the reception of cases of so-called shell shock. I don't think there is any group of cases so pathetic as these. I saw a ward with perhaps 25 soldiers, who were all victims of this terrible condition. They stand up when the physician makes his rounds. Most of them had continuous tremor with staring eyes, a look of terror and blue, cold extremities. When examined, they show various manifestations which we are not apt to attribute to hysteria. Some are deaf and dumb and some are dumb. The disorders of the special senses are most remarkable. The condition is described under various names, such as shell psychasthenia or shell neurasthenia, but it is commonly called shell shock. So far as one can judge, they look on the whole to be rather inferior types both physically and mentally. I was told they were of the type that cannot stand alcohol and were total abstainers in about 80% of the cases. Two of the patients had never been wounded. There has been a good deal of discussion as to how many of the patients may be malingerers, and this has to be considered most carefully. There is no doubt an element of malingering in some of them, but it is impossible that the greater majority of them should be of this type. These conditions are tremendously interesting to the psychologists. I found Dr. Sherrington of Oxford devoting much attention to them. He called them disassociation of special senses. Meyer's view is that they are inhibitions from a tremendous disturbance of the consciousness of the personality of the individual, so that various nervous tracts are blocked for the time being. Some of the patients are treated by hypnotic suggestion with a good deal of success. Dr. Sherrington was telling me of a case in which the patient had been anesthetized and was cured by the anesthesia. Sometimes, when the patients go under the anesthetic, they regain their speech, and sometimes they begin to talk when they are coming out of it. Then they can continue to speak.

Of course, the great problem of the war is the handling and treatment of wounds. I came into contact with that when I reached Paris. The following day I went out to the American Ambulance Hospital at Neuilly. This is an institution of which we should be very proud. Not that we are doing enough, for we are not beginning to do enough along these lines, but it is a splendid institution, splendidly managed, and splendid work is done there. I saw nothing finer. They started at first with the system of changing units. The Harvard unit went there and I think the Chicago unit also. This was a bad system undoubtedly and has been abandoned in the Harvard Hospital, which is to have permanent heads. Obviously it is not a good plan to be constantly having one group of men go and another group replacing them. I understand that Dr. Hugh Cabot is going back as the permanent head of the Harvard Hospital in the district of Boulogne. The American Ambulance is more or less permanent. One side is more or less French, and the rest of the hospital, the more active part, is under Dr. Hutchinson of Philadelphia. He is doing splendid work, and it is a great inspiration to see him. There

is one doctor at the American Ambulance who simply went over to see things, but who became so absorbed he never left. That is the right spirit, and when one considers not only the scientific and professional interest, but the tremendous human interest as well, it is not surprising he stayed. There is a good laboratory there, with one of our younger men as an assistant. It was at the American Ambulance that I learned at first hand, for the first time, of the various methods and ideas regarding wound treatment. The wounds are to a large extent infected by bits of shrapnel or shell. There are some bullet wounds. Some of the types, which Dr. Cushing has described so well, are most interesting, where the men, particularly the Australians, cannot keep their heads down in the trenches, but will look over, and the bullet cuts right across the top of the skull.

I may say there is no conceivable injury which is not inflicted in this war. When I went to Boulogne to visit Sir Almroth Wright, one man said to me: "You must not go without looking at some of my cases. You will never have such a chance again." He showed me a case of Brown-Séquard's paralysis from an injury. One might indeed go through life without seeing a case where just one-half of the spinal cord was cut across. It is a wonder to me that more of those who can go are not over there to acquire some practical experience.

To return to the treatment of wounds. They are nearly all infected. The bacterial flora of the wounds is carefully studied. There, of course, is a wonderful field which is by no means exhausted. The bacillus which we worked with here many years ago, the gas bacillus responsible for gas gangrene, is seen in nearly all of the wounds. The results which are obtained in the treatment of wounds seem to be on the whole fairly good, so far as I could judge. Unquestionably the most brilliant results are those of Carrel at his hospital at Compiègne, an exceedingly interesting hospital about 50 miles out of Paris, with no very heavy fighting going on in front. Verdun is on the east and the Somme on the west. Dr. Carrel is at the end of a salient with great preparations for the reception of wounded. Thousands of men are provided for in that region. Carrel has relatively few cases as compared with the more active hospitals, but his results are surprising. As I understand it, the general principles which guide him, and most of them, are these: First, a very thorough opening up of the wound, with the removal of all foreign material, dead tissue, torn and lacerated tissues, etc. The cleansing of the wound follows and it is that part which takes time. This is done at Carrel's hospital with unusual care and is perhaps better managed there than anywhere else. Then comes the irrigation of the wound. Some think it a matter of indifference as to which irrigating fluid is used, but not so Carrel. His theory is that he is actually sterilizing the wound and the disinfectant which he uses is Dakin's solution, which has been modified to some extent by the use of bicarbonate of soda to render it less irritating. There is nothing new, of course, about the solution, but this is the prevailing disinfectant. After that there is an ingenious arrangement of small elastic tubes, connected with a single tube, which is attached to an irrigating bottle. These are inserted into the wound. By Carrel's method, it is necessary for the nurse to flood the wound every two hours. Then throughout from the start there is a bacteriological control. The determination of the behavior of the bacteria under the influence of this treatment is made from smears, usually from every part of the wound. At Carrel's laboratory the methods are very thorough. Everything is charted and worked out mathematically. The surgeons determine when the wound can be closed by the disappearance of the bacteria. Carrel spoke of sterile wounds. I suspect that cultures could still be grown, but the wounds are sterile surgically. You will say: "What is new about that?" There is nothing new in any one thing, but I think there is something new in the thoroughness with which the method is carried out in every step. If you go through Carrel's hospital and see his work, you feel that he is making a perfectly definite contribution, and although you may not accept his theories, you can see that his results are better than those elsewhere. Over there, some of them attribute it to the fact that he gets better cases, perhaps only two or three hours old, whereas in some hospitals the wounds are two or three days old when received. He also has a superior hospital, with the necessary funds. Whatever it may be, he obtains these results, which I think would impress anyone. Sometimes, in from 36 to 48 hours the wounds are all closed up, and they get beautiful clean scars from these bruised, lacerated wounds, so one cannot but feel that Carrel has made a real contribution. Dr. Hutchinson, at the American Ambulance, knew about it and he had made up his mind to introduce the Carrel methods in every detail.

Dr. Blake is at Ris-Orangis, and seems to have very sane views on everything. His great contribution is the treatment of fractures, and his results are very remarkable. I did not see any ward which looked just like his. He has good appliances which looked very ingenious, by which extremities are put into every conceivable position necessary to bring the parts into the right relation with each other. He is always trying out various methods. He told me he thought that one method is better for one stage of the disease and another method for another, and that in changing from one to the other good results are obtained.

One of the most interesting things is the part played by dentists there. At the American Ambulance there are rooms filled with dental chairs. This is a very essential part of the work. Every hospital I saw had some dental work, but none in which it was carried out so wonderfully as at the American Ambulance.

The removal of foreign bodies has become a definite specialty. I heard the other night of one surgeon who does nothing but go around to different hospitals and remove foreign bodies with extraordinary deftness. Most surgeons do not believe in removing foreign bodies, claiming that they do not do any harm. This man has a deftness which is said to be most wizard-like. The foreign body is located by X-ray pictures taken at different angles. He then goes in with extraordinary accuracy. He has a little electric magnet device at the end of his finger, with a telephone attachment to the ear. When he is within a certain distance of the foreign body it registers on the telephone.

There is not time to speak of many interesting and important things, such as trench fever. I hardly believe that this is an ordinary streptococcic infection. It is not typhoid fever, nor paratyphoid fever. It is very probably a new disease, not identical with any we have had before. It is a relapsing fever, and some think it may be conveyed by insects or lice, like typhus.

Surgical shock is a fascinating subject. Dr. Porter, professor of physiology at Harvard, has been living in the trenches studying shell shock. I saw him a few days ago in Boston and asked him to come down here and tell us of his experiences, which he promised to do.

Venereal diseases are a terrible scourge and everybody is quite awake on the subject.

I have occupied more time than I should, but I have only touched upon some of the experiences. I would like to add this. The problems are of intense interest and whatever your particular line may be—surgical, medical, bacteriological or physiological—I am convinced there is some field there which will prove of absorbing interest. If you have an opportunity to go there and avail yourself of this unique experience, you certainly should do so. I think it would be surprising if any surgeon who had the chance did not jump at the opportunity. I would say the same thing to young men who are more interested in the laboratory side of the work or in medical problems.

Dr. Watson: What is the nature of the poisonous gas?

Dr. Welch: I am afraid you will have to ask the Germans that. It is believed to be mainly chlorine. Various kinds have been used, but chlorine, I think, has been most commonly employed. It is regarded still as the worst, although perhaps not the most deadly. I might say that some of the physiologists are directing their attention towards protection against gas poisoning. It is now provided against quite satisfactorily and is not of great consequence any longer.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB.

NOVEMBER 13, 1916.

1. **On the Etymology, Popular and Scientific, of the Term for Kidney in Various Languages.** Dr. D. I. Macht.
   To appear later in the Bulletin.
2. **Prehistoric Pathology—Paleopathology.** Dr. Arnold C. Klebs.
   To appear later in the Bulletin.

NOTES ON NEW BOOKS.

London, Oxford Medical Publications: Cerebrospinal Fever. By Thomas Horder, R. A. M. C. Cloth, $1.25. (*Henry Froude and Hodder & Stoughton, 1915.*)

Medical Hints. By Col. J. Edward Squier, R. A. M. C. Cloth, $1.00. (*Henry Froude and Hodder & Stoughton, 1915.*)

Abdominal Injuries. By Prof. Rutherford Morison and Lieut. Col. W. G. Richardson, R. A. M. C. Cloth, $1.00. (*Henry Froude and Hodder & Stoughton, 1915.*)

Wounds in War; Their Treatment and Their Results. By Lieut. Col. D'Arcy Power, R. A. M. C. Cloth, $1.00. (*Henry Froude and Hodder & Stoughton, 1915.*)

These small Oxford War Primers deserve the attention of civilian medical men who are liable for army service. In his volume on cerebrospinal fever, Horder gives an excellent presentation of this disease as observed by him during the epidemic in England during the first year of the war, with a consideration of the special features presented by the disease among soldiers. The serum treatment is recommended as the most valuable means of combating the epidemic, and emphasis is laid on its early use as well as on the great importance of early isolation and prophylaxis.

In his *Medical Hints* Col. Squier gives some excellent suggestions to the civilian physician who is called to active service. He emphasizes the great care which must be taken in the selection of recruits and careful observation of their training in order to produce an efficient fighting force. Since the true function of the medical officer is the prevention of disease, a large part of the book is taken up with suggestions as to prophylaxis. The efficiency of the troops being absolutely dependent on their marching ability Squier emphasizes the importance of the care of the feet and gives valuable suggestions as to the prevention of trench frost-bite which has made necessary the withdrawal of so many otherwise healthy soldiers.

In *Abdominal Injuries*, Morison and Lieut. Col. Richardson discuss the symptoms and types of abdominal injuries caused by different kinds of projectiles and the indications for operation. They believe that "all abdominal injuries should be operated on, but only in properly equipped hospitals." Owing to the efficiency of the Royal Army Medical Corps they state that the majority of patients can be brought in six hours to a well-equipped hospital where abdominal operations can be undertaken. Of penetrating abdominal injuries 20 per cent are hopeless, but with early operation 60 per cent of the remaining patients should recover. The technique of abdominal operations is discussed but the author's recommendations would find but few advocates among American surgeons. He is in favor of flushing the peritoneal cavity with salt solution and the use of the Murphy button when resection is necessary. No mention is made of the often life-saving measure of enterostomy, either as a primary procedure or in the treatment of post-operative complications.

Lieut. Col. D'Arcy Power in his *Wounds in War* is an advocate of Watson-Cheyne's technique of cauterization with carbolic acid, but states that this treatment is only suitable for wounds seen forty-eight hours after injury. Little emphasis is placed on Wright's views and the physiologic basis claimed for them, and no mention is made of Dakin's solution. The types of wounds caused by the different projectiles are well discussed, and valuable suggestions made for treatment *en route* to the wounded man's final destination. The author lays special emphasis on free incision for all infected wounds. A whole chapter is given over to the vaccine treatment, but little emphasis is laid on the importance of routine injection of the wounded for the prevention of tetanus. In his brief discussion of this disease the author makes no mention of magnesium sulphate, which has proven of so much value.

I. A. C. C.

Harvey's Views on the Use of the Circulation of the Blood. By Dr. John G. Curtis, M. D. Cloth. (*New York: Columbia University Press, 1915.*)

This book, which represents Dr. Curtis' translations and his ideas about Harvey, has been published under the editorial supervision of Dr. Frederick S. Lee. In the different chapters are taken up in succession the various points about the circulation in relation to the tissues and respiration, until the author finally works up to the actual demonstration of the return circulation. Perhaps the most interesting chapter is the fourth, in which the first recorded mention of the movement of the blood in a circle is shown in a photograph of the page from Harvey's lecture notes of 1616. Everywhere throughout the text there are splendid translations of Harvey's writings. At the end of the book, there is a long list of notes for reference from the text, which will enable the student to trace out the exact source of information on all the points mentioned.

J. A. C.

Modern Medicine and Some Modern Remedies. By Dr. Thomas Bodley Scott. Cloth, $1.50. (*New York: Paul B. Hoeber, 1916.*)

This little book, although written for the general practitioner, is to be recommended to the student, first of all, on account of the interesting preface by Sir Lauder Brunton. Any student that contemplates taking up general practice, and who knows the type of work that is before him, can be helped a great deal by reading this little essay. Dr. Scott writes in a very interesting manner, his introduction laying stress upon the difference between hospital and private practice. The section on the diagnosis and treatment of cardiac disorders is well written. There is an interesting chapter on therapeutic speculations and doubts, in which the functions of the glands of internal secretion, more particularly, and their therapy are considered. On the whole the book is well worth reading.

J. A. C.

NEW PUBLICATIONS.

The following monograph is for sale by The Johns Hopkins Press, Baltimore, Md.:

Relation of Tonsillar and Nasopharyngeal Infections to General and Systemic Disorders. By S. J. Crowe, S. Shelton Watkins and Alma S. Rothholtz. 63 pages. Price, $1.25.